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SULFONAMIDE COMPOUNDS IN THE PREVENTION AND TREATMENT OF WOUND INFECTION

A CONSIDERATION OF THE PRINCIPLES WHICH GOVERN THEIR USE

PERRIN H. LONG, M.D.
BALTIMORE

The introduction of the use of sulfonamide compounds as prophylactic and curative agents in the field of surgery has not been an unmitigated blessing for surgeons because of a growing tendency to neglect fundamental principles of good surgical judgment and technic and to rely instead on the wholesale use of the "wonder drugs." This undesirable condition has been brought about by a false impression that the sulfonamide compounds are "cure-alls" and represents a current trend toward an ignorant complacency in respect to the elective and selective uses of these agents.

There can be no questioning the fact that these drugs have frequently saved the patient of the careless surgeon from disaster, but when the sulfonamides fail because of neglect of the use of sound judgment and surgical technic, coupled with a lack of knowledge of the fundamental principles of sulfonamide therapy, then too often these drugs are berated as being worthless, when the truth of the matter is that the primary principles of the surgical aspects of the patient's care have been cast aside. One must remember (and too often in the present this fact is being forgotten) that the use of sulfonamide compounds is an adjunct to surgical therapy and cannot replace it. However, these drugs can be valuable aids when properly employed and have permitted the development of certain advances in surgical practices which were considered unattainable before the advent of sulfanilamide and its derivatives.

With the establishment of the proposition that sulfonamide therapy is a valuable adjunct to adequate surgical treatment, the problem of their use in the prophylaxis and therapy of contaminated and infected wounds becomes simplified. In civilian practice it has been established that many contaminated wounds can be closed directly after an adequate toilet of the wound has been completed. However, in war wounds (except for very minor lacerations) experience has shown that primary closure is dangerous, and with few exceptions (perforations of the chest or abdomen) such wounds should be left open. It is of interest to recall at this point that the adequate use of locally implanted sulfanilamide in the wounds of our casualties in Hawaii prevented wound infection, thereby permitting the débridement of some wounds many hours after they had been incurred. Then after a few days the wounds were so clean that some were secondarily sutured and healing by first intention occurred.[1] Infected wounds should always be left open.

In any consideration of the use of sulfonamide compounds in the prophylaxis or treatment of wound infection, several factors must be considered, and among these are the type of surgical procedure employed, the condition of the wound at the completion of surgical treatment, the determination of whether oral and/or local sulfonamide therapy will be used, the proper selection of the drug for peroral or local use, the dosage to be used, the duration of treatment and finally the utilization of the correct postoperative care in order that the greatest benefits may be derived from the employment of the sulfonamide compounds.

It has been established that the sulfonamides can be used in the treatment of wounds regardless of the type of surgical procedure that has been employed. As far as is known at the present time, the administration of these drugs is compatible with the use of standard intravenous, inhalant or local anesthetics, and they will not influence adversely either the course or the treatment of traumatic or infectious shock.

The condition of the wound at the time sulfonamide therapy is used is of importance. Obviously a poorly debrided, carelessly drained fresh wound is an unsuitable site for the implantation of the sulfonamides, and under such conditions the drugs may eventually fail to exert their prophylactic effect. The method of wound closure is important. Implanted sulfonamide compounds may cause an exudation of tissue fluids into the wound, and sloughing of the wound edge has been noted as a result of the tension created by these fluids when wounds have been closed too tightly. This possibility should be kept in mind when one is dealing with lacerations in which especial consideration must be given to the final cosmetic effect. It has been shown [2] that necrotic material or pus contains sulfonamide inhibitors; hence every effort should be made to eliminate and neutralize these substances before sulfonamide therapy is started.

The experience of the last few years has shown that oral, topical or oral plus topical medication with the sulfonamides will prevent wound infection. However, the best evidence available at the present time shows that the administration of these drugs by the peroral

From the Department of Preventive Medicine, Johns Hopkins University School of Medicine.
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1. Moorhead, J. J.: Surgical Experience at Pearl Harbor, J. A. M. A. **118:** 712 (Feb. 28) 1942. Ravdin, I. S., and Long, P. H.: Army M. Bull., April 1942, no. 61, p. 1; U. S. Nav. M. Bull. **40:** 353 (April) 1942.

2. Lockwood, J. S.: J. Immunol. **35:** 155 (Sept.) 1938. Lockwood, J. S., and Lynch, H. M.: Studies on Mechanism of Action of Sulfanilamide: Influence of Proteolytic Products on Effectiveness of Sulfanilamide, J. A. M. A. **114:** 935 (March 16) 1940; Surgery **10:** 493 (Sept.) 1941.

and local routes is to be desired in the prophylaxis of infection in moderate or serious wounds of the soft tissue, compound fractures, compound skull or faciomaxillary injuries and penetrating wounds of the abdomen or chest. Infection can generally be prevented in minor lacerations involving the skin and subcutaneous tissues or superficial muscle layers, without extensive destruction of tissue, by the topical application of a sulfonamide compound.

In the selection of the drug of choice for the peroral prophylaxis or therapy of wound infection, the effectiveness of the drug and its toxicity are primary considerations. It has been shown that sulfadiazine is clinically effective against systemic infections produced by staphylococci, hemolytic streptococci, colon bacilli and members of the aerogenes group. In clostridial infections this drug has been proved active against experimental infections produced by Clostridium perfringens or Clostridium septicum. It offers a wide range of protection against the common primary contaminating and infecting organisms in wounds.

A recent survey which we have made of the occurrence of the important toxic reactions (fever, rash, acute hemolytic anemia, leukopenia, acute agranulocytosis, renal complications and hepatitis) of sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine shows that a total of 11.9 per cent of such reactions occur in the course of sulfanilamide therapy, 15.9 per cent when sulfapyridine is employed, 18.6 per cent if sulfathiazole is used and but 6.5 per cent when therapy is conducted with sulfadiazine.

In addition, sulfadiazine produces comparatively little nausea and vomiting and rarely any degree of cyanosis; mental disturbances and incoordination are uncommon; endurance is not seriously affected, and acidosis or a lowering of the plasma carbon dioxide content does not occur. The lack of these side effects is of importance in any consideration of the ambulatory wounded and in the transportation by air of injured patients. Against these favorable factors is the known ability of the drug to produce renal damage. Observations made by my associates and me show that one can expect that in about 1.7 per cent of patients receiving average doses of this drug either microscopic or gross hematuria will develop while in 0.4 per cent oliguria, azotemia or anuria develops. It is known that a decreased fluid intake with a resulting decrease in the output of urine predisposes a patient to this type of renal complication. Hence, when water is scarce, as in desert warfare, or when temperatures are high and loss of body water is great, the threat of kidney damage might be considered a deterrent to the use of sulfadiazine. However, the occurrence of this complication appears to be greater when sulfapyridine or sulfathiazole is administered, and one must remember that sulfanilamide produces hemolytic anemia in about 2 per cent of patients to whom it is given. After an evaluation of the various factors involved, it seems reasonable to conclude that, while sulfadiazine can produce serious toxic reactions, it is the least toxic of the four commonly used sulfonamide drugs and is the drug of choice for the peroral prophylaxis of contaminated wounds and for the peroral therapy of infected wounds. If sulfadiazine is not available, sulfanilamide or sulfathiazole should be used in the order named in the peroral prophylaxis or therapy of contaminated or infected wounds.

Confusion exists in respect to the topical use of sulfonamide compounds. For example it is commonly assumed that because sulfathiazole is more effective than sulfanilamide in the systemic therapy of staphylococcic infections, its topical use is always indicated when the possibility or the presence of staphylococcic infection exists. This assumption is not necessarily correct because various factors such as the physical characteristics and solubility of the drug, its antibacterial effect in the upper ranges of its solubility, its rate of diffusion and absorption from the local lesion, the effect produced by its local implantation on tissue repair and wound healing and the systemic toxic effects which the drug may produce enter into any consideration of the selection of the drug of choice for topical use in the prevention or treatment of contaminated or infected wounds.

It has often been observed that when too finely powdered sulfonamide compounds are placed in wounds they tend to "cake." Sulfonamide compounds for topical use, consisting of large crystals or coarsely ground forms of these drugs, dissolve slowly in wounds and tend to initiate foreign body reactions. While the ideal crystal size of these compounds is not definitely known, it has been shown that satisfactory results can be obtained when crystalline sulfanilamide screened to 40 to 80 mesh is used.

The solubility and diffusibility of the compounds under consideration for local use is of importance. Sulfanilamide is soluble in tissue fluids to the extent of from 1,200 to 1,500 mg. per hundred cubic centimeters and has been shown by Hawking [3] to diffuse rapidly through living tissue and fairly well through dead tissue. This observer has demonstrated that sulfathiazole, sulfapyridine and sulfadiazine are much less soluble (184, 61 and 124 mg. per hundred cubic centimeters in human serum at 36 C. respectively) than is sulfanilamide and that sulfapyridine and sulfathiazole diffuse more slowly through living tissues. In our experience sulfadiazine behaves like sulfapyridine as far as diffusion is concerned. This variation in the solubility of the drugs is important in estimating the possible antibacterial effects of these compounds when they are employed as topical agents, and it has been shown in vitro that in the upper range of its solubility sulfanilamide seems to be as effective an antibacterial agent as are the other sulfonamide compounds at their limits of solubility. This observation is important in the consideration of the sulfonamide drug of choice for local use in the prophylaxis and treatment of wound infections.

As has been pointed out, sulfanilamide diffuses more rapidly from the site of its implantation than do the other sulfonamides, and following the topical use of crystalline sulfanilamide in closed wounds peak concentrations of the drug in the blood can be expected in from six to twelve hours, with absorption and excretion of the drug being practically completed within forty-eight hours unless massive doses of sulfanilamide have been used locally. The peak concentrations of this drug in the blood are considerably higher than those noted following the local use of sulfathiazole, sulfapyridine or sulfadiazine in wounds that are closed.

The latter compounds, because of their lower solubilities and rates of diffusion, are absorbed and excreted more slowly than is sulfanilamide, and in the instance of sulfadiazine we have noted that following the implantation of 5 Gm. of the drug in an extraperitoneal wound of the abdominal wall absorption of the drug continued for more than two weeks.

3. Hawking, Frank: Lancet 1:786 (June 21) 1941.

There is not a great deal of information available regarding the absorption of sulfonamide compounds from open wounds. Veal and Klepser [4] have reported that the instillation of 7.5 Gm. of sulfanilamide into an "open clean wound (pilonidal sinus excision)" produced a peak concentration of the drug of 2 mg. per hundred cubic centimeters within five hours and at forty-two hours very small amounts (less than 0.5 mg. per hundred cubic centimeters) of the drug were found in the blood. Another of their patients suffering from an open wound of the abdominal wall was given the daily implantations of 5 Gm. of sulfanilamide, followed by a gradual rise of the concentration of the drug in the blood to 12 mg. per hundred cubic centimeters on the sixth day. At the end of thirty-six hours the concentration of sulfanilamide in the blood was 3 mg. per hundred cubic centimeters. These observations, coupled with those of our own, lead us to believe that excessive concentrations of sulfanilamide are not to be expected following its use in open wounds. In burns, the opposite seems to be true. Hooker and Lam [5] have shown that when crystalline sulfanilamide is applied to second or third degree burns absorption may be rapid and excessive concentrations of the drug may occur in the blood. Our own observations show that sulfathiazole and sulfadiazine are less readily absorbed from open wounds than is sulfanilamide.

The differences in the solubility of the various sulfonamide drugs appear to bear some relation to their effects on wound healing. It has been shown [6] that in concentrations up to approximately 500 mg. per hundred cubic centimeters, sulfanilamide has little if any effect on the multiplication of fibroblasts in tissue cultures and that, while this drug does inhibit certain cellular functions in higher concentrations, the recovery of the cells from its unfavorable action is rapid and complete when they are removed from excessive concentrations of the drug. Sulfathiazole [7] has been shown to be the least favorable for growth at any assigned concentration, and as far as sulfapyridine and sulfadiazine are concerned their limited solubility does not permit the accurate testing of their effects on cells in tissue cultures.

It seems well established that the degree of solubility of the various sulfonamide drugs has a definite bearing on their ability to produce foreign body reactions when they are implanted locally. Sulfanilamide, because of its high solubility, is least likely to produce this reaction within wounds, with sulfathiazole, sulfapyridine and sulfadiazine in the order named having increasing possibilities of producing such a reaction.

As far as direct toxic effects on various types of tissue are concerned, there is disagreement concerning the action of the sulfonamide drugs. Russell and Falconer [8] reported that the application of finely powdered sulfanilamide or sulfapyridine to the leptomeninges or the cortex of the rabbit did not produce appreciable damage within four days. Hurteau [9] has confirmed and extended these observations and has further reported that while sulfadiazine is slowly absorbed from brain tissue no glial reaction occurs after the implantation and but a slight foreign body reaction in the meninges. Taffel,[10] on the other hand, has noted that all of the commonly used sulfonamides produced a mild inflammatory reaction when applied to the cortex in monkeys. Sulfathiazole seemed to produce the most intense inflammatory response, while sulfadiazine caused the most severe foreign body reaction. These observations are of especial interest in view of the recent report of Watt and Alexander.[11] These observers noted that the application of crystalline sulfathiazole to the frontal cortex in both human beings and dogs frequently produced epileptiform convulsions. This phenomenon did not occur when sulfanilamide, sulfapyridine or sulfadiazine was used.

Taffel and Harvey [12] reported that the local application of crystalline sulfanilamide did not interfere with the healing of experimental wounds in the stomachs of rats. Harbison and Key [13] have confirmed this observation and have further reported that the implantation of crystalline sulfanilamide did not disturb the healing of wounds produced in the abdominal walls of rats, nor did this drug produce adhesions when introduced into the peritoneal cavity of rats.

Glynn [14] states that crystalline sulfanilamide has "a slight but definite toxic reaction on striped muscle," but that this drug does not inhibit fibroblastic proliferation in wounds produced in rabbits. Taylor,[15] however, has reported that all these drugs produce inflammatory tissue reactions when implanted into wounds in dogs and that in the case of the less soluble drugs the reactions may be so severe that actual tissue destruction and sterile abscess formation occurs. Finally, Bick [16] has recently observed that "the local application of sulfonamide drugs to wounds of the soft tissues or cleancut operative incisions in which primary suture is indicated retards healing by at least 50 per cent of the time factor and promotes extensive cutaneous scarring."

As has been previously described, the local application of the sulfonamide drugs to wounds may cause an exudation of tissue fluids, which in the instance of a tightly sutured wound may cause tension and delay wound healing. Our observations lead us to believe that sulfathiazole and sulfadiazine are more likely to produce such an exudation of fluid than is sulfanilamide.

Out of the welter of conflicting experimental and clinical reports which I have just reviewed one fact seems to emerge, namely that, while the local implantation of sulfanilamide may interfere to a certain degree with wound healing it appears to be the least harmful of the commonly used sulfonamides to regenerating tissues.

Thus when all the factors have been considered, it seems reasonable to choose sulfanilamide as the drug of choice for the prophylaxis and treatment of contaminated and infected wounds.

In considering the peroral prophylactic dose of sulfadiazine needed for the prevention of wound infections, civilian injuries must be differentiated in general from war casualties. In the first instance, definitive surgical treatment will probably be given promptly and in most cases the administration of sulfadiazine by mouth can

4. Veal, J. R., and Klepser, R. G.: M. Ann. District of Columbia **10:** 61 (Feb.) 1941.
5. Hooker, D. H., and Lam, C. R.: Surgery **9:** 534 (April) 1941.
6. Gey, G. O.: Personnal communication to the author. Jacoby, Medawar and Willmer.[7]
7. Jacoby, F.; Medawar, P. B., and Willmer, E. N.: Brit. M. J. **2:** 149 (Aug. 2) 1941.
8. Russell, R. S., and Falconer, M. A.: Lancet **2:** 100 (July 27) 1940.
9. Hurteau, E. F.: Canad. M. A. J. **46:** 15 (Jan.) 1942.
10. Taffel, Max, and German, W. J.: Yale J. Biol. & Med. **14:** 139 (Dec.) 1941.
11. Watt, A. C., and Alexander, G. L.: Lancet **1:** 493 (April 25) 1942.
12. Taffel, Max, and Harvey, S. C.: Proc. Soc. Exper. Biol. & Med. **47:** 202 (June) 1941.
13. Harbison, S. P., and Key, J. A.: Local Implantation of Sulfanilamide and Its Derivatives in Wounds: Its Relation to Wound Healing and to Peritoneal Adhesions, Arch. Surg. **44:** 22 (Jan.) 1942.
14. Glynn, L. E.: J. Path. & Bact. **53:** 183 (Sept.) 1941.
15. Taylor, F. W.: Misuse of Sulfonamide Compounds, J. A. M. A. **118:** 959 (March 21) 1942.
16. Bick, E. M.: Observations on Topical Use of Sulfonamide Derivatives, J. A. M. A. **118:** 511 (Feb. 14) 1942.

be deferred until just prior to or after definitive surgical treatment. In the case of persons wounded as the result of enemy action, definitive surgical treatment may be delayed for many hours; therefore, the prophylactic dose of sulfadiazine should be given as soon as possible after the wound has been incurred.

For adult civilian injuries, the initial peroral dose of sulfadiazine should be 2 to 4 Gm. given either immediately before or after definitive surgical treatment, this to be followed by 1 Gm. of the drug every six hours for two days, following which doses of 0.5 Gm. every six hours should be administered for eight days.

For adults wounded as the result of enemy action, the initial peroral dose of sulfadiazine should be 4 Gm. This should be given as soon as possible. After this initial dose no more of the drug should be given by mouth until after definitive surgical treatment has been completed. Then sulfadiazine 1 Gm. every six hours should be administered day and night for from seven to ten days. If infection occurs despite the attempt at prophylaxis, the administration of the drug should be continued until the infection is under control. It is important to maintain a daily output of urine of at least 1,000 cc. during the period of treatment in order to lessen the possibility of the occurrence of renal complications. If sulfadiazine is not available, sulfanilamide or sulfathiazole prescribed in the same dosage may be used. For injured children doses of these drugs should be adjusted according to the weight of the child in comparison with the adult dose.

There is a tendency at the present time to dump sulfonamide compounds haphazardly into wounds. This is a bad practice, and it should be emphasized that the implantation of sulfanilamide should be done carefully in order that all parts of the surface of the exposed wound will be in contact with the drug. A shaker-top container makes this easy, although many physicians prefer to use a powder atomizer for applying sulfanilamide locally.

In wounds that are closed by primary suturing, the amount of crystalline sulfanilamide implanted should approximate 0.05 Gm. per square inch of wound surface. This represents a light "frosting" of the wound. In contaminated wounds in which closure is not indicated, or in infected wounds, 0.1 Gm. of crystalline sulfanilamide per square inch (2.5 cm.) of wound surface should be used. This represents a heavy "frosting" of the wound. On the basis of our present experience it would seem that not more than 10 Gm. of sulfanilamide should be given locally to any given patient within a twenty-four hour period.

The combination of sulfadiazine by mouth and sulfanilamide locally will produce sulfonamide concentrations in the blood of from 6 to 16 mg. per hundred cubic centimeters in the first twenty-four hours in patients whose wounds are closed. If, however, the wounds are left open, concentrations of the sulfonamide in the blood of from 5 to 10 mg. per hundred cubic centimeters will generally be noted in the first twenty-four hours of therapy.

It has been mentioned previously that peroral therapy with sulfadiazine may be discontinued in from seven to ten days if symptoms and signs of infection are lacking. However, experience has repeatedly shown that it is necessary to repeat the local application of sulfanilamide to wounds at each dressing period if both primary and secondary wound infection is to be prevented. Local therapy with sulfanilamide should be continued until healing is complete.

As has been pointed out before, the successful treatment of contaminated or infected wounds is influenced by the amount of necrotic tissue or purulent material in the wounds, because these substances act as sulfonamide inhibitors. Therefore, if a wound shows evidence of infection it should be gently irrigated with isotonic solution of sodium chloride at each dressing or, perhaps better, with a mild oxidizing agent such as a 1:3,300 solution of azochloramid. (Such solutions should be stored away from the light in brown glass bottles.) It has been shown that the latter compound is effective in neutralizing the effects of sulfonamide inhibitors, and indeed there is some evidence [17] that azochloramid acts synergistically with the sulfonamides. Recent experience has also shown the value of utilizing dressings moistened with a 1:3,300 solution of azochloramid in the prophylaxis of contaminated and the treatment of infected wounds. These dressings can be placed in the wound after crystalline sulfanilamide has been applied and sealed over with boric acid ointment or petrolatum gauze to prevent them from drying. It is important to keep the wound dressing moist in order to prevent the caking of implanted sulfonamides.

Other substances have been reported as being effective in removing the effects of the sulfonamide inhibitors found in pus and necrotic material. Veal and Klepser [4] used allantoin in combination with sulfanilamide in an ointment base and reported that this mixture stimulated the growth of healthy granulation tissue. Holder and MacKay [18] have reported that a carbamide-sulfanilamide mixture gave excellent results when used in the local prophylaxis and treatment of contaminated or infected wounds.

SUMMARY AND CONCLUSIONS

The use of sulfonamide compounds for the oral and topical prophylaxis or treatment of contaminated or infected wounds is a valuable adjunct to careful surgical treatment but cannot replace it. However, the rational use of the sulfonamides has permitted the development of certain advances that were considered unattainable before the advent of sulfanilamide and its derivatives.

The broad general principles which govern the chemotherapy of wounds are applicable regardless of the anatomic location of the wound. On the basis of present evidence, it would seem that a combination of systemic with local therapy offers the best chance for the prevention of wound infection and for its cure once an infection has become established. On the basis of current evidence, sulfadiazine by mouth seems to be the drug of choice for systemic therapy, and the dose of the drug should be adjusted so that concentrations of from 4 to 7 mg. per hundred cubic centimeters are obtained in the blood. Higher concentrations of the drug are probably unnecessary. From all points of view, sulfanilamide seems at the present time to be the drug of choice for topical application. It is to be remembered that necrotic tissue and pus contain sulfonamide inhibitors and that every effort should be made to eliminate these inhibitors before sulfanilamide is applied locally. Care should always be taken to prevent the caking of sulfanilamide in the wound, and this can be accomplished by applying moist gauze dressings following the application of sulfanilamide to the wound. In the absence of clinical infection, there is little reason to continue oral therapy with sulfadiazine for more than five to seven days. However, to prevent secondary

17. Schmelkes, F. C., and Wyss, O.: Proc. Soc. Exper. Biol. & Med. **49**: 263 (Feb.) 1942.
18. Holder, H. G., and MacKay, E. M.: Mil. Surgeon **90**: 509 (May) 1942.

infections from occurring after primary prophylaxis has been successful, it is necessary to apply sulfanilamide powder locally until wound healing is complete.

615 North Wolfe Street.

ABSTRACT OF DISCUSSION

DR. JOHN E. CANNADAY, Charleston, W. Va.: My experience with sulfonamide compounds in wounds has been that both sulfanilamide and sulfathiazole may be used satisfactorily in both clean and infected wounds, that they lower the incidence of infection in both types of wound and that when used in moderation they do not cause appreciable delay in wound healing. I spread these drugs evenly throughout the wound and, in the case of sulfathiazole, rub it into the tissues in order to avoid the formation of lumps such as others have described. It has been well established that sulfanilamide, when used in wounds, is completely absorbed in the course of about two days and that under similar conditions sulfathiazole requires five or six days for absorption. Likewise it has been amply demonstrated that if sulfathiazole is placed in the wound in lumps or masses it probably will not be entirely absorbed and may act as a foreign body. A recent check-up on 1,281 consecutive abdominal surgical cases of myself and my associates in the surgical service of the Charleston General Hospital, the general surgical technic being the same in all cases, shows that of 910 uninfected wounds closed with cotton thread used in accordance with the Halsted silk technic there were 7 infections, or 0.77 per cent. Of 129 uninfected wounds closed with catgut there resulted 8 infections, or 6 per cent. Of contaminated wounds, 175 sutured with cotton, there were 30 infections, or 17 per cent. Of 31 contaminated wounds closed with catgut there were 8 infections, or 26 per cent. All these wounds, both uninfected and contaminated, were irrigated thoroughly with saline solution and either sulfanilamide or both sulfanilamide and sulfathiazole were placed in them. In this series there were 18 gastric resections for ulcer with no apparent infections but with 1 wound disruption which followed a persistent cough. This disruption was closed soon after it took place and healed without infection. In the entire series of uninfected wounds there were approximately 12 that had a brief serous leakage for a few days but healed without pus formation. While we cannot expect everything from the use of sulfonamide compounds in wounds, we do believe that when used in conjunction with adequate hemostasis, wound irrigation or accurate suturing (especially with cotton thread) they definitely help to lower the incidence of infection in both uninfected and contaminated wounds, and that if infection does follow their use the severity is at least lessened.

DR. PHILIP LEWIN, Chicago: I should like to ask Dr. Long to discuss combinations of the sulfonamide compounds and their use in ointments, in tetanus, in gas gangrene and in burns.

DR. PERRIN H. LONG, Baltimore: Combinations of these drugs for local use such as sulfanilamide plus sulfadiazine or sulfathiazole have to be handled much more carefully; otherwise one will get the adverse effects of the less soluble drugs. I further believe that the evidence from Pearl Harbor shows that sulfanilamide by itself is an adequate chemoprophylactic agent against wound infection. Sulfonamide ointments are of value in the treatment of infected wounds. I don't know anything about their use in prophylaxis of wound infection, but in superficially infected wounds sulfonamide ointments are effective, and I should think that the ointment described by Dr. Vella, in which there is hydrous wool fat, would be a satisfactory ointment. Zinc peroxide is excellent in the treatment of anaerobic or microaerophilic infections. Technically it would be difficult to use adequately in the prophylaxis of wound infection if there were large numbers of casualties. As far as we know, there was no tetanus in Hawaii from military casualties. Gas gangrene serum has not been conclusively proved to be of value in either the prophylaxis or the therapy of clinical clostridial infection. What we need for the treatment of burns is a method which every one of us can use and get good results. Unfortunately no method gives good results when used by all physicians. The one that comes closest in the opinion of many who are interested in burns in this country is tannic acid, but, as every one knows, that does not represent the perfect treatment.

SULFONAMIDE TOXICITY AS A CAUSE OF DEATH IN NEW YORK CITY IN 1941

W. D. SUTLIFF, M.D.
Assistant Director (Pneumonia), Bureau of Laboratories, New York City Department of Health
MILTON HELPERN, M.D.
Assistant Medical Examiner, New York City Medical Examiner's Office
GERARD GRIFFIN, M.D.
Consultant on Pneumonia Therapy, New York City Department of Health
AND
HERBERT BROWN, B.S.
Statistical Clerk, New York City Department of Health
NEW YORK

It is imperative that comprehensive information on the frequency of fatal sulfonamide reactions be obtained in order that the physician may employ the sulfonamide drugs with a definite knowledge of the dangers involved in their administration. To fill this need, the Pneumonia Control Division of the New York City Department of Health [1] and the Bureau of Vital Records and Statistics cooperated with the New York City Chief Medical Examiner's Office to obtain clinical records for all deaths in New York City during 1941, in which some type of sulfonamide toxicity was a factor.

SOURCES OF REPORTS [2]

The medical examiner's certification provided the greatest proportion of useful records, namely 16 out of 19. Such certification includes a critical examination of the clinical history furnished by the physician or institution and in some cases postmortem examination. Reports received by the health department without the intervention of the medical examiner provided a smaller proportion of useful records, namely 9 out of 17. In these cases either sulfonamide administration was mentioned on the death certificate but was not definitely stated as responsible for death or the case was recorded in a scientific publication. A questionnaire on sulfonamide toxicity to physicians reporting pneumonia deaths during parts of April and May 1941 gave only a small number of useful reports, namely 4 out of 21 cases that were studied because serious toxic symptoms were reported on the questionnaire. One of these 4 cases had been reported and certified by the medical examiner before its report by questionnaire. The primary function of the questionnaire was to serve as a check on the completeness of the reporting from the two other sources.

CRITERIA FOR THE DIAGNOSIS OF SULFONAMIDE TOXICITY AS A CAUSE OF DEATH

Twenty-eight cases were selected for description and analysis in this report. All presented toxic reactions which developed coincident with drug administration. In each case the reaction was of a type produced by sulfonamide drugs and was considered the sole or a contributory cause of death.

In 13 cases, the diagnosis was as well established as present knowledge permits. These include 5 cases of

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1. Drs. M. J. Hanigsberg, S. H. Taylor and Arnold Treitman, New York City Department of Health, pneumonia control division consultants in pneumonia therapy, assisted by abstracting clinical records.

2. Three of these cases (5, 14 and 15) were described by other authors.

agranulocytosis (1, 2, 3, 4 and 5), 1 case of acute hemolytic anemia (9), 2 cases of purpura hemorrhagica (11 and 12), 4 cases of crystalline urinary concretions (13, 14, 15 and 16) and 1 case of dermatitis exfoliativa assigning a cause of death. Such cases are essential to a discussion of the incidence of deaths related to sulfonamide toxicity. Questions as to the pathogenesis of the toxic condition might be raised in 12 of the 15

TABLE 1.—*Cases of Fatal Sulfonamide Toxicity Reported in New York City in 1941*

Patient	Age	Sex	Principal Reaction	Drugs	Total Amount, Gm.	Disease Treated	Cause of Death
			A. Toxicity Primarily Affecting the Blood Cells and Blood Forming Organs				
1. A. G.	53	♂	*Agranulocytosis	Sulfanilamide	103	Infected foot (diabetic gangrene)	Agranulocytosis
2. C. H.	50	♂	*Agranulocytosis	Sulfanilamide (33.32 Gm.) Sulfapyridine (84.0 Gm.)	117	Bacterial endocarditis (Strep. viridans)	Agranulocytosis, bacterial endocarditis
3. L. W. V.	68	♂	*Agranulocytosis	Sulfathiazole	98	Cystitis	Agranulocytosis, prostatic hypertrophy (operation), peritonitis
4. C. S.	44	♀	*Agranulocytosis	Sulfanilamide (in wound 60.0 Gm.) Sulfathiazole (24.5 Gm.)	84	Infected operative wound, cystitis	Agranulocytosis, cancer of sigmoid (operation), bronchopneumonia
5. R. F.	13	♂	*Agranulocytosis	Sulfanilamide (53.1 Gm.) Sulfathiazole (intravenous 3.8 Gm.)	57	Rheumatic fever inactive	Agranulocytosis, septicemia, Staphylococcus aureus, Pneumococcus type 3
6. A. M.	19	♀	Agranulocytosis	Sulfanilamide	50	Pharyngitis	Agranulocytosis, bronchopneumonia
7. F. M.	65	♀	Agranulocytosis	Sulfapyridine	16	Upper respiratory infection	Agranulocytosis
8. R. E. M.	60	♀	Agranulocytosis	Sulfathiazole (12.0 Gm.) Neoprontosil (17.0 Gm.)	29	Tonsillitis	Agranulocytosis, aminopyrine 7 Gm.
9. C. G.	43	♂	*Acute hemolytic anemia, hemoglobin nephrosis	Sulfanilamide	10	Infected accidental wound	Acute hemolytic anemia, hemoglobin nephrosis, pneumonia
10. M. R.	45	♂	Aplastic anemia	Sulfathiazole	7	Lobar pneumonia, type 18	Aplastic anemia, type 18 pneumonia, bacteremia
11. B. H.	66	♀	*Purpura hemorrhagica	Sulfathiazole	12	Lobar pneumonia	Purpura hemorrhagica
12. N. F.	60	♀	*Thrombocytopenic purpura	Sulfadiazine	24	Infected operative wound	Thrombocytopenic purpura (operation), Staph. aureus, sepsis
			B. Toxicity Primarily Affecting the Kidney				
13. C. T. V.	45	♀	*Crystalline urinary concretions	Sulfathiazole	35	Lobar pneumonia, type 3	Renal obstruction, crystalline concretions, uremia
14. H. K.	60	♂	*Crystalline urinary concretions	Sulfathiazole	44	Postoperative pneumonia	Renal obstruction, crystalline concretions, uremia, bronchopneumonia
15. R. N.	15	♀	*Crystalline urinary concretions	Sulfathiazole	18.5	Acne	Renal obstruction, crystalline concretions, uremia
16. C. N.	80	♀	*Crystalline urinary concretions	Sulfadiazine	128	Lobar pneumonia, type 2 (not confirmed)	Uremia, pyelitis, chronic cholecystitis and lithiasis
17. E. C. D.	65	♂	Acute nephrosis	Sulfathiazole	28	Carbuncle of neck	Acute nephrosis, uremia
18. M. McG.	56	♀	Acute nephrosis	Sulfapyridine	14	Bronchopneumonia	Acute nephrosis, uremia
19. F. R.	48	♂	Azotemia	Sulfathiazole (intravenous)	24	Postoperative pneumonia	Uremia, bilateral renal calculi, operation, peritonitis, pneumonia
20. W. J. D.	57	♂	Azotemia	Sulfathiazole	40	Pneumonia (not confirmed)	Uremia, chronic hypertension, cardiovascular disease, pulmonary edema
21. N. L.	65	♂	Azotemia	Sulfadiazine	27	Bronchopneumonia	Uremia, hypertension, nephrosclerosis
22. L. K.	56	♀	Azotemia	Sulfapyridine	31	Bronchopneumonia	Uremia, chronic nephritis (histoscopy), bronchopneumonia
23. P. M.	39	♀	Azotemia	Sulfapyridine	12	Pneumonia	Uremia, arteriosclerosis, nephritis
24. G. B.	70	♂	Azotemia	Sulfathiazole	29	Infected chronic leg ulcers	Uremia
			C. Toxicity Primarily Affecting the Skin and Other Toxic Manifestations				
25. E. A. W.	31	♀	*Dermatitis exfoliativa	Sulfapyridine	24	Gonorrheal vaginitis	Dermatitis exfoliativa
26. J. M.	42	♂	Dermatitis hyperpyrexia	Sulfathiazole (intravenously 6 Gm.)	70	Lobar pneumonia	Sulfathiazole toxicity, lobar pneumonia
27. R. P.	59	♂	Dermatitis, pulmonary edema	Sulfathiazole (38 Gm.) Sulfapyridine (11 Gm.) (39 Gm. intravenously)	88	Bronchopneumonia	Sulfonamide toxicity, bronchopneumonia, pneumonoconiosis
28. M. L.	11 mos.	♀	Convulsions	Sulfathiazole (7.2 Gm.) Sulfapyridine (1.2 Gm.) (0.5 Gm. intravenously)	9	Bronchopneumonia	Convulsions due to intravenous administration of sodium sulfapyridine; bronchopneumonia

* Diagnosis well established.

(25). In 5 of these 13 cases the toxic reaction was the sole cause of death.

The remaining 15 cases, in which the diagnoses were merely acceptable, are included in this report because they represent a reasonable application of our knowledge of sulfonamide toxicity to the difficult problem of acceptable cases, namely 3 cases of agranulocytosis (6, 7 and 8) and 1 case of aplastic anemia (10) because blood counts were not recorded before the conditions were recognized, 2 cases of acute nephrosis (17 and 18) because this condition has not received adequate critical study, 6 cases of azotemia (19, 20, 21, 22, 23 and 24)

because no complete mechanical obstruction of the urinary tract was recognized, and in 5 of the latter because some evidence of other kidney disease was present. Questions as to whether the toxic manifestations were severe enough to cause death might be raised in 3 of the 15 acceptable cases (26, 27 and 28), in which reactions of types not heretofore described occurred in cases in which intravenous therapy was administered for pneumonia and in which the pneumonia as well as in the seventh decade of life. The 4 exceptions were 1 infant of 11 months and 3 young adults of 13, 15 and 19 years of age. They were equally divided as to sex into 14 males and 14 females. Characteristic features of the reactions are listed in tables 1 and 2.

Types of Principal Reactions and Drugs Administered.—The symptoms of toxicity affected primarily the blood cells and blood forming organs in 12 of the 28 cases (table 1, section A). Of these 8 had agranulo-

TABLE 2.—*Number of Days Elapsing Before the Development of Toxicity and Death*

Patient	Principal Reaction	Other Toxic Symptoms	Drugs	Days of Treatment	Number of Days from First Dose of Drugs to: First Toxic Symptoms	Number of Days from First Dose of Drugs to: Principal Toxic Reaction	Number of Days from First Dose of Drugs to: Death
		A. Toxicity Primarily Affecting the Blood Cells and Blood Forming Organs					
1. A. G.	Agranulocytosis	Fever,* dermatitis	Sulfanilamide	20	18	21	23
2. C. H.	Agranulocytosis	Fever (due to endocarditis ?)	Sulfanilamide (8 days)	31 (89 day period)	..	88†	94
			Sulfapyridine (23 days)	..	..	22‡	28
3. L. W. V.	Agranulocytosis	Fever,* dermatitis	Sulfathiazole	17	17	22	22
4. C. S.	Agranulocytosis	Fever,* dermatitis	Sulfanilamide (in wound 37 days)	37	31	35	37
			Sulfathiazole (7 days)	..	..	..	15
5. R. F.	Agranulocytosis	Fever, angina (due to sepsis)	Sulfanilamide (31 days in 32 days)	32 (in 35 day period)	29	32	35
			Sulfathiazole (intravenously 1 day)				
6. A. M.	Agranulocytosis	Fever (due to bronchopneumonia ?)	Sulfanilamide	16 (19 day period)	..	23	25
7. F. M.	Agranulocytosis	Fever (due to respiratory infection ?)	Sulfapyridine	3	..	2	14
8. R. E. M.	Agranulocytosis	Fever (due to tonsillitis ?)	Sulfathiazole (2 days) Neoprontosil (3 days)	5	..	4	9
9. C. G.	Acute hemolytic anemia	None	Sulfanilamide	1	..	1	10
10. M. R.	Aplastic anemia	Fever (due to pneumonia ?)	Sulfathiazole	2	..	6	23
11. B. H.	Purpura hemorrhagica	None	Sulfathiazole	2	..	5	7
12. N. F.	Thrombocytopenic purpura	Fever (due to sepsis ?)	Sulfadiazine	6	..	6	8
		B. Toxicity Primarily Affecting the Kidney					
13. C. T. V.	Crystalline urinary concretions	Fever,* dermatitis, chill, delirium, convulsions	Sulfathiazole	8	7	9	11
14. H. K.	Crystalline urinary concretions	Fever,* chill,* dermatitis, sulfathiazole retention	Sulfathiazole	10	8	11	14
15. R. N.	Crystalline urinary concretions	General aches and pains,* vomiting, delirium, fever,* convulsions	Sulfathiazole	31	30	32	33
16. C. N.	Crystalline urinary concretions*	Sulfadiazine retention	Sulfadiazine	22	..	22	22
17. E. C. D.	Acute nephrosis	Fever,* chill,* dermatitis	Sulfathiazole	13 (15 day period)	11	16	25
18. M. McG.	Acute nephrosis	Fever,* dermatitis, delirium	Sulfapyridine	4 (5 day period)	3	6	10
19. F. R.	Azotemia	.....	Sulfathiazole (intravenously)	5	..	2	5
20. W. J. D.	Azotemia	Urticaria*	Sulfathiazole	5	5	7	39
21. N. L.	Azotemia	Oliguria,* severe emesis	Sulfadiazine	6	5	6	11
22. L. K.	Azotemia	Oliguria	Sulfapyridine	8	..	7	11
23. P. M.	Azotemia	Coma *	Sulfapyridine	3	3	7	12
24. G. B.	Azotemia	Fever,* dermatitis,* sulfathiazole retention	Sulfathiazole	6	7	12	14
		C. Toxicity Primarily Affecting the Skin and Other Toxic Manifestations					
25. E. A. W.	Dermatitis exfoliativa	Fever	Sulfapyridine	16 (19 day period)	..	23	38
26. J. M.	Dermatitis, hyperpyrexia	.....	Sulfathiazole (intravenously on 11th day)	11	..	11	12
27. R. P.	Dermatitis, pulmonary edema	Jaundice	Sulfathiazole (7 days) Sulfapyridine (9 days, some intravenously)	15	..	15	16
28. M. L.	Convulsions	Hyperpyrexia (due to bronchopneumonia ?)	Sulfathiazole (9 days in 11 days) Sulfapyridine (2 days) (0.5 Gm. intravenously 11th day)	10 (in 13 day period)	..	12	13

* Indicates first toxic symptoms observed. † Sulfanilamide. ‡ Sulfapyridine.

other concurrent disease were present at death. In 5 of the 15 acceptable cases the toxic reaction was considered the sole cause of death. Autopsy protocols were studied and confirmed the diagnosis in 8 of the 13 well established cases and in 4 of the 15 cases that were considered merely acceptable.

DESCRIPTION OF REACTIONS

The 28 patients presenting the diagnosis of sulfonamide toxicity associated with death were, with 4 exceptions, 31 years of age or over, the largest number being

cytosis, 1 acute hemolytic anemia, 1 aplastic anemia and 2 purpura hemorrhagica. Each of the common sulfonamide drugs, used alone or in combinations with other sulfonamide drugs, accounted for one or more of these reactions. Agranulocytosis followed the administration of one drug in 4 cases, i. e., sulfanilamide in 2, sulfapyridine in 1 and sulfathiazole in 1, and agranulocytosis followed the administration of two drugs in 4 cases, in one of which sulfanilamide and sulfapyridine were administered, in 2 sulfanilamide and sulfathiazole

and in 1 azosulfamide, sulfathiazole and aminopyrine. The 1 case of acute hemolytic anemia followed sulfanilamide. One case of aplastic anemia followed sulfathiazole. Purpura followed sulfathiazole in 1 case and sulfadiazine in another.

Toxicity primarily affected the urinary tract in 12 of the 28 cases (table 1, section B). Obstruction by crystalline concretions occurred in the ureters, kidney pelves or kidney tubules in 4 of these cases. Acute degenerative nephrotic lesions almost entirely confined to the tubular epithelium, without evidence of obstruction by crystalline concretions, were found in 2 cases. Azotemia increasing progressively to death appeared following sulfonamide drugs in 6 cases, in 5 of which some evidence of previous renal damage due to other disease was also present. Three cases of crystalline urinary concretions followed sulfathiazole administration, and 1 followed sulfadiazine. One case of acute nephrosis followed sulfapyridine, and 1 followed sulfathiazole. Two cases of azotemia followed sulfapyridine, 3 followed sulfathiazole and 1 followed sulfadiazine.

The remaining 4 of the 28 cases in which sulfonamide toxicity was diagnosed, and related to the cause of death, constitute a miscellaneous group of reactions that have been the subject of few or no reports in the medical literature. The first of these 4 patients had dermatitis exfoliativa, the second patient had acute generalized dermatitis and hyperpyrexia, the third patient developed acute generalized dermatitis and pulmonary edema. The fourth patient was an 11 month old infant girl who had convulsions and hyperpyrexia. The first patient had received sulfapyridine, the second sulfathiazole and the third and fourth both sulfapyridine and sulfathiazole. The 3 cases with acute dermatitis and fever all followed unusually large doses of the drugs, part of which was administered intravenously, and death occurred within twenty-four hours of the appearance of toxic symptoms.

No cases of death from acute liver degeneration following the use of sulfonamide drugs were reported in New York City in 1941.

In the whole series of 28 cases sulfanilamide was used in 6 cases, azosulfamide in 1, sulfapyridine in 8, sulfathiazole in 16 and sulfadiazine in 3. One drug only was used in 22 cases and two drugs in 6 cases.

Drug Dosage.—There is a tendency for serious toxic reactions to follow doses of sulfonamide drugs that are greater than those usually required for therapeutic effect. Twenty of the 28 patients received 20 Gm. or more of sulfonamide drugs. The dosage of sulfonamide drugs was highest in the first 6 patients with agranulocytosis, all of whom received 50 Gm. or more. Drug dosage was also high in 3 patients who had reactions characterized chiefly by drug fever and rash, 2 adults who received 70 Gm. or more, and an 11 month old girl who received 8.9 Gm. In 1 case with renal toxicity 128 Gm. was given but in the remaining 11 cases with renal toxicity the drug dosage was lower, ranging from 12 to 44 Gm. In the 6 remaining cases, in 5 of which the blood was affected by the toxic reaction, and in 1 case of dermatitis exfoliativa, the dosage was even lower, ranging from 7 to 24 Gm. per case.

Number of Days Elapsing Before the Development of Toxic Reactions.—The number of days from the beginning of sulfonamide administration to the appearance of toxic symptoms and death tended to be similar in individuals with certain reactions (table 2). Agranulocytosis in 6 cases was recognized twenty-one or more days after the drugs were begun. In the 2 remaining cases of agranulocytosis the intervals between the beginning of treatment and recognition of toxicity were very short, two and four days respectively; but in these cases blood counts were not made before treatment was begun, and the possibility that agranulocytosis was present even before drug administration should not be overlooked. Acute hemolytic anemia appeared within twenty-four hours of the first dose of sulfanilamide. Aplastic anemia and purpura hemorrhagica were recognized on the fifth or sixth day after therapy was begun. Toxicity primarily affecting the kidney was recognized at variable periods after therapy began, up to thirty-two days, most often at the end of the first week. Dermatitis exfoliativa was recognized twenty-three days after sulfonamide therapy was begun. Acute toxemia in patients receiving intravenous sulfonamide drugs appeared about the end of the second week of treatment of 3 patients.

Fatal termination followed the first symptoms of toxicity in 6 of the cases of agranulocytosis at an interval of five or six days. In the 2 remaining cases of agranulocytosis death occurred in two and twelve days respectively, after recognition of agranulocytosis. One case each of acute hemolytic anemia and aplastic anemia resulted in death ten and seventeen days respectively after they were recognized. Two cases of purpura hemorrhagica, on the other hand, had very short durations, death occurring in two days in both. Renal toxicities were variable in duration, ranging from one to nine days in all but 2 cases, in which the durations were fourteen and thirty-four days respectively. The 1 case of dermatitis exfoliativa resulted in death fifteen days after the skin reaction was first recognized. In the 3 cases of sulfonamide reactions in which the drugs were administered intravenously death occurred acutely within twenty-four hours after onset of the reactions.

Drug and Fever Skin Reactions.—These alone or in combination preceded other signs of drug toxicity in 9 cases. One or both of these symptoms were present in a total of 14 of the 28 cases, in 3 of 8 cases of agranulocytosis, in 3 of 4 cases in which crystalline urinary concretions were present, in 2 cases of acute nephrosis, and in all 4 miscellaneous cases in which a cutaneous reaction or hyperpyrexia were an essential part of the principal toxic reaction. In only 2 of 6 cases of azotemia was drug fever or cutaneous reaction present. In 7 of the remaining 14 cases in which toxicity affected the blood, fever occurred which could not be distinguished from that due to the disease under treatment, while in 7 there were no sustained fever and no cutaneous reactions. When one or both of these two symptoms are attributed to drug toxicity their possible association with other serious toxic manifestations should be considered.

Diseases for Which Sulfonamide Drugs Were Administered.—Pneumonia treatment was responsible for 14 of the 28 cases reported in this series. This predominance was especially pronounced in the 12 cases of toxicity affecting the kidney, in 9 of which treatment was given for pneumonia. Gonorrhea, on the other hand, was the disease under treatment in only 1 case. The infrequency of toxic reactions in the treatment of gonorrhea has been noted by others and has been

attributed to the relatively small doses of sulfonamide drug administered for gonorrhea. Other diseases for which sulfanilamide treatment was given were local infections 3 cases, upper respiratory infections 3 cases, infected surgical wounds 2 cases, bacterial endocarditis 1 case, cystitis 1 case, carbuncle 1 case, acne 1 case and rheumatic fever 1 case.

FREQUENCY OF DEATHS DUE TO SULFONAMIDE TOXICITY

Experience shows that case reporting is rarely complete. More complete reporting of sulfonamide toxicity was therefore sought by specific inquiries to physicians and hospitals reporting deaths due either to primary pneumonia or to pneumonia classified as secondary to another disease. Pneumonia was chosen as the subject of the questionnaire because treatment of pneumonia is the commonest source of reports of fatal sulfonamide toxicity. Questionnaires were sent out for 1,000 consecutive cases and filled out and returned for 993. One or more sulfonamide drugs were administered in 645 of these. Complete case records were studied for 20 that presented the most serious toxic symptoms. In 1 the diagnosis of sulfonamide toxicity was well established (11, purpura hemorrhagica), and in 3 evidence for the diagnosis of sulfonamide toxicity associated with death was acceptable (7, agranulocytosis, 22, azotemia and 23, azotemia). Four of these cases are included in the 28 cases of fatal sulfonamide toxicity. Only 1 of these 4 fatal cases of sulfonamide toxicity (7) had been reported through ordinary channels before the questionnaire was submitted. Evidence was therefore obtained that reporting by the usual methods was not complete. A rough calculation of the degree of completeness may be made by comparing the proportion of the cases of fatal sulfonamide toxicity among the pneumonia deaths the subject of questionnaire with the proportion of cases of fatal sulfonamide toxicity reported as occurring in cases of pneumonia among the estimated total number of cases in the city in which sulfonamide treatment was administered. The ratio of toxic deaths in the questionnaire was 4 in 645, or 1 death due to sulfonamide toxicity in 161 pneumonia deaths. The ratio for the city as a whole was 8 in 5,480 estimated pneumonia deaths,[3] or 1 death due to sulfonamide toxicity in 685 pneumonia deaths. In one borough with the best record of case reporting, however, the ratio was 5 fatal reactions in an estimated 1,778 pneumonia deaths in cases in which sulfonamide drugs were administered, or 1 death due to sulfonamide toxicity in 356 pneumonia deaths. These calculations confirm our impression that reporting of sulfonamide deaths by the ordinary methods is incomplete but that it can be increased considerably under certain conditions.

The questionnaire also furnished additional information as to the frequency with which drugs were employed. During this period sulfathiazole was the drug most often used for the treatment of pneumonia. Sulfathiazole was given in 329, or 51 per cent, of the 645 cases, sulfapyridine in 168, or 26.1 per cent, sulfanilamide in 23, or 3.8 per cent, sulfadiazine in 18, or 2.8 per cent, and more than one drug in 107, or 16.6 per cent. Despite the frequent use of sulfathiazole, only 1 of the 4 cases of sulfonamide toxicity associated with death revealed by the questionnaire followed sulfathiazole, while 3 followed the use of sulfapyridine. It has been noted, however, that sulfathiazole was the drug most often administered in the 27 cases described. This may have been due merely to the more frequent use of sulfathiazole during this period in the treatment of disease. There is no evidence in this study that sulfathiazole is more often followed by fatal toxicity than the other commonly used sulfonamide drugs.

3. Estimated to correspond with those considered in the questionnaire as follows: 3,380 recorded primary pneumonia deaths times 2.49 equals an estimated total of 8,431 deaths in which pneumonia was the primary or contributory cause; 65 per cent of 8,431 equals 5,480, the number of pneumonia deaths in which it is estimated that sulfonamide treatment was given.

SUMMARY

The 28 reported cases of sulfonamide toxemia associated with death conform to one standard of diagnosis. They were reported almost entirely by ordinary methods in one year in a city in which a total of 74,553 deaths from all causes occurred, or approximately 1 fatal case of sulfonamide toxicity in every 2,571 deaths from all causes. One fatal sulfonamide reaction was reported by ordinary means among every 685 estimated pneumonia deaths. The highest frequency was found to be 1 sulfonamide death among 161 reported pneumonia deaths by supplementary inquiries on sulfonamide toxicity to physicians reporting deaths from pneumonia. Since the present fatality rate of pneumonia is in the neighborhood of 10 per cent, it may be estimated that there is as many as 1 sulfonamide death for every 1,610 pneumonia cases in which sulfonamide drugs are employed. These numbers are believed to be as near to the actual incidence of death due to sulfonamide toxicity as one may approach by ordinary methods of reporting at this time. Difficulties encountered in making positive assertions as to causes of death in such cases are illustrated by the necessity for considering the diagnosis as well established in some cases and merely acceptable in others. Such diagnostic difficulties must often deter physicians from reporting sulfonamide toxicity as a cause of death. It was therefore assumed that reporting would be incomplete, and this assumption was substantiated by the results of the questionnaire. The incidence of sulfonamide toxicity associated with death as found here is an improvement on previous data because of the relatively large numbers involved, and it is therefore useful despite its known incompleteness as a basis for discussing the present significance of sulfonamide deaths. These data will also be of value as a comparative figure for other similar studies.

COMMENT

Although few individual physicians treat enough patients with sulfonamide drugs to make the risk of fatalities approach certainty within periods of one or even several years, every physician using sulfonamide drugs runs some risk of observing such a fatality among his own patients. The serious problem presented by the combination of great therapeutic value with definite toxic hazards must be faced by the profession.

The frequency of fatal sulfonamide toxicity makes it necessary to consider the possibility of reducing their numbers. Measures are being actively sought to avoid serious toxic reactions, but so far with little success. It seems possible, however, that the use of less drug in each case would prevent the occurrence of some reac-

tions. Emphasis on early diagnosis of susceptible infections and early treatment with resulting more rapid and more complete therapeutic effects is the most desirable method of decreasing the amount of drug needed in each case. It is not advisable to change standard dosage schedules which are known to be successful, since they are based on experimental demonstration of the necessity for certain minimum blood levels of the drugs for maximum therapeutic effect.

Even after the onset of toxic symptoms, measures may be taken to reduce the number of fatalities. Early recognition of serious toxic symptoms, followed by prompt cessation of drug therapy, is of considerable importance. Symptomatic therapy, such as transfusion in blood dyscrasias, alkalization of urine in hemoglobin nephrosis and instrumental relief of gross urinary tract obstruction may also save some patients. But symptomatic therapy can be only partially successful, and some fatal toxic reactions will continue to occur. It is to be hoped that biochemists will develop therapeutic agents which are less toxic or devise ways of lessening the toxic effects of present drugs.

The frequency of fatal sulfonamide toxicity makes it necessary to consider whether the beneficial results of sulfonamide drug therapy are sufficient to justify the continued use of these drugs as now practiced. Since low fatality rates have been shown to result from sulfonamide therapy in many infections, the changes in reported deaths from diseases for which sulfonamide drugs are now used should give some indication as to whether lives are actually being saved. Striking changes have occurred in the number of reported deaths in New York City from the fourteen following infections for which sulfonamide drugs are used to treat the infection itself, to treat predisposing conditions, or to treat serious complications: cerebrospinal (meningococcic) meningitis, scarlet fever, erysipelas, measles, meningitis (not meningococcic), diseases of the ear and mastoid process, pneumonia (all forms), empyema, diseases of the pharynx and tonsils, appendicitis, abortion with mention of infection, infection during childbirth and through the puerperium, phlegmon and acute abscess, and osteomyelitis and periostitis. It is estimated that if the average mortality rate from these causes of 137.5 deaths per hundred thousand of population during the five years 1932 through 1936, before the introduction of sulfonamide drugs had persisted through 1941, 10,341 deaths would have occurred instead of the 4,475 reported, a difference of 5,866 deaths.[4] While the number of deaths from many of these diseases was decreasing before this period and were subject to other influences than the introduction of sulfonamide drugs, it may reasonably be assumed that some part of the decrease in each of these conditions was due to sulfonamide therapy. It is safe to say that the number of lives saved by sulfonamide drugs in New York City in 1941 was very much greater than the number of deaths caused by the toxic action of these drugs.

Bacterial endocarditis presents a special application of sulfonamide drug treatment, because the disease is almost invariably fatal and therefore fatalities which appear to be due to the drug are also usually considered due in part to the disease. The number of recoveries resulting from drug therapy is, however, small, and it would be well to demonstrate that the number of recoveries from sulfonamide treatment of bacterial endocarditis is greater than the number of cases in which serious terminal toxic reactions occur in evaluating drug therapy of this disease.

In acute gonococcic infections, few or no lives are saved; but since 85 per cent of the cases result promptly in cure by one course of a relatively small dose of sulfathiazole, the prospect of eradicating this disease is considered well worth the few serious toxic reactions that result from sulfonamide treatment.

Our present satisfactory experiences with sulfonamide treatments encourage their extension to other diseases. Such extensions should be based on therapeutic trial carried out to assemble clear information as to therapeutic and toxic effects. Such extension may, however, be directed toward the prevention of sequelae of the disease under treatment, the prevention of infections resulting from operative procedures, the prevention of recurrences of disease such as acute rheumatic fever or toward the cure of the carrier state for various pathogenic bacteria. It is essential that such preventive use of sulfonamide drugs should be considered successful only when fatal toxic reactions are entirely avoided.

This study of fatal toxic reactions following the use of sulfonamide drugs in one year in New York City presents no evidence that would modify the course that is being pursued in the routine use and in the experimental extension of the use of sulfonamide drugs. The benefits derived from this course are much greater than the risk of serious toxic reactions incurred.

4. To be published.

ABSTRACT OF DISCUSSION

DR. PERRIN H. LONG, Baltimore: Dr. Sutliff and his co-workers are to be congratulated because theirs is the first attempt to find out how many people have died as the result of treatment with sulfonamide compounds. Some of our more pessimistic friends were not completely right, as the report shows, that sulfonamide therapy is not a leading cause of death. This study brings up another question. What is happening to our population from the point of view of becoming sensitized to sulfonamide drugs? Recently I reviewed many figures dealing with the incidence of sulfonamide toxicity in adults and, if one considers fever, rash, acute hemolytic anemia, leukopenia, granulocytopenia, hematuria, oliguria, azotemia, anuria and liver damage as the important toxic reactions, one finds that with sulfanilamide one gets a total of 11.9 per cent complication, with sulfapyridine 15.9 per cent, with sulfathiazole 18.6 per cent and with sulfadiazine 6.5 per cent. These percentages are based on records from thousands of adults and probably are statistically correct. In 1941 there were probably about 750,000 pounds of sulfapyridine produced in this country, 1,200,000 pounds of sulfanilamide and between a million and million and a half pounds of sulfathiazole. A certain amount of this production was used in veterinary medicine, a small amount in dentistry and a fair amount was exported, but that still leaves a great deal of the sulfonamides for use in this country. One can judge that somewhere in the neighborhood of 10 to 15 million people received one of the sulfonamide derivatives last year. With this in mind, and with our knowledge of the frequency with which sensitivity to these drugs arises, it shows that these drugs should not be administered unless definite indications for their use is present; otherwise we shall gradually sensitize a large section of our population. The authors stressed the question of the relation of the size of the dose to the occurrence of toxic reactions. There can be no question that there is a definite relation between the amount of the drug administered to the occurrence of toxic reactions, but there is also another factor, especially with granulocytopenia, namely the time factor. A survey of the literature (there are about 250

cases of granulocytopenia from sulfonamide compounds reported) shows that with but few exceptions this toxic reaction occurs after the twelfth day of treatment. That is why the total dosage often seems great. If one determines incidence in respect to time, one will find that granulocytopenia occurs most frequently between the seventeenth and the twenty-fifth day of treatment, with the earliest case occurring in the first week and the latest cases occurring as late as the sixtieth or seventieth day of treatment.

DR. RUSSELL L. CECIL, New York: Dr. Sutliff and his co-workers have made an important contribution to the subject of sulfonamide intoxication as a cause of death. It is clear from their figures that a great majority of the fatal reactions from sulfonamide treatment result either from damage to the kidneys or from depression of the hemopoietic system. In my experience renal damage has usually taken the form of crystalline obstruction in the pelves or tubules, but apparently a nephrosis or even a nephritis with azotemia may also occur. We must not forget, however, that many of the infections, such as pneumonia, in which sulfonamide therapy is used, are capable of producing, by themselves, considerable tubular and glomerular damage. It is quite possible, therefore, that the sulfonamides in such cases may occasionally augment an already damaged tissue. The fatalities resulting from injury to the hemopoietic system may result from granulocytopenia or less frequently from hemorrhagic purpura and aplastic or hemolytic anemia. I was particularly interested in Dr. Sutliff's reference to those cases of granulocytopenia which had developed in 6 cases twenty-one or more days after the drug was begun. These delayed reactions are something we must keep in mind, and their occasional occurrence makes it necessary to watch the blood for several weeks after the drug treatment has been discontinued. It is also obvious from Dr. Sutliff's study that any one of the four commonly used sulfonamides may be responsible for a fatal reaction. Toxic reactions are much less prevalent with sulfadiazine than with the other sulfonamides, but already a number of deaths have been reported from sulfadiazine therapy. Dr. Norman Plummer has determined the incidence of toxic reactions in 1,000 patients treated in our wards at the New York Hospital with sulfadiazine or sodium sulfadiazine. One hundred and five of these patients showed some form of toxic manifestation, but the great majority of these were of a very mild character. Renal irritation, skin rashes and drug fever made up the greater number of the reactions, and none of these were of a serious nature. The one fatal reaction was a thrombocytopenic purpura. Strangely enough, the only fatal reaction which I have encountered in private practice was also due to hemorrhagic purpura. This occurred in a middle aged man with lobar pneumonia and followed the administration of about 40 Gm. of sulfapyridine. Finland has recently reported 445 cases in which sulfadiazine therapy was employed with no deaths. His percentage of toxic reactions was about the same as that observed by Dr. Plummer. Perhaps the surest way to avoid fatal toxic reactions is to use the minimum amount of drug necessary to control the infection.

The Average Doctor.—'Honour the physician with the honour due unto him for the uses which ye may have of him.' So wrote Jesus Ben Sira, the son of Sirach. The usefulness of the doctor, then, is his mark of distinction, and the wish to spend his life in a useful manner is probably the closest approach to altruism that most physicians achieve. There are some, undoubtedly, who hear the call to minister to humanity as a sacred duty, and if they are sincere they are worthy of special respect; but an intimate acquaintance with the medical profession leads me to believe that the average doctor has neither more nor less nobility of character than has the average decent citizen of the same breeding, environment and education; he simply happens to be more interested than are they in helping people to get well; that is his work, and he loves it, but it is not his religion.—Irving, Frederick C.: Safe Deliverance, Boston, Houghton Mifflin Company, 1942.

THE SODIUM SALTS OF SULFAPYRIDINE, SULFATHIAZOLE AND SULFADIAZINE

THEIR CLINICAL USE BY HYPODERMOCLYSIS

FIRST LIEUTENANT GEORGE V. TAPLIN
MEDICAL CORPS, ARMY OF THE UNITED STATES
FIRST LIEUTENANT EDWARD A. CUSTER
MEDICAL CORPS, ARMY OF THE UNITED STATES
AND
LAWRENCE E. YOUNG, M.D.
ROCHESTER, N. Y.

In a previous communication from this clinic[1] the use of sodium sulfapyridine by hypodermoclysis was discussed. Our purpose in this paper is to describe in more detail our experience with the subcutaneous use of the sodium salts of sulfathiazole and sulfadiazine in addition to that of sulfapyridine and to emphasize that these drugs may be administered safely and conveniently by hypodermoclysis. During the past three years the aforementioned sulfonamide compounds have been administered by this route in 160 cases of pneumonia and other conditions for which this group of drugs was indicated but in which oral administration was difficult or impossible. More recently concentrations of these drugs in the blood have been followed at frequent intervals after hypodermic administration in 19 of these cases. The results of these studies are presented here.

METHOD OF PREPARATION AND ADMINISTRATION OF SULFONAMIDE SOLUTIONS

The majority of the patients were treated with 0.5 per cent sodium sulfonamide solutions made by dissolving 5 Gm. of the sodium sulfonamide in 1 liter of isotonic solution of three chlorides, isotonic solution of sodium chloride or one-sixth molar sodium lactate solution. Concentrations of the sulfonamide compounds as high as 0.8 per cent were used. Isotonic solution of sodium chloride was the vehicle most commonly employed.

The solutions were prepared in one of the following ways: 1. The sodium sulfonamide was added to the vehicle and the mixture heated to the boiling point and allowed to cool to body temperature before administration. 2. The vehicle was first heated to the boiling point and allowed to cool slightly and then the drug was added. After cooling, the solution was ready for use. The first method is the more convenient, but either may be used without apparent difference in blood concentration or therapeutic response.

The p_H values of the sulfonamides in saline solution as determined by the Beckman apparatus were as follows: sodium sulfapyridine 10.0, sodium sulfathiazole 9.5, and sodium sulfadiazine 9.2. In spite of the decided alkalinity, these solutions caused no local reactions when injected under the skin.

The solutions described were injected into both thighs by hypodermoclysis over periods of from two to five hours. Some patients were given an initial intravenous injection of from one fifth to one third of the prepared 0.4 per cent to 0.8 per cent sulfonamide solution over a twenty to thirty minute period. The remain-

Dr. N. L. Kaltreider assisted the authors in this study.
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From the Department of Medicine, University of Rochester School of Medicine and Dentistry, and the Medical Clinics of the Strong Memorial and Rochester Municipal hospitals.

1. Taplin, G. V.; Jacox, R. F., and Howland, J. W.: Use of Sodium Sulfapyridine by Hypodermoclysis, J. A. M. A. **114**: 1733 (May 4) 1940.

ing portion of the solution was then given by hypodermoclysis.

From 19 patients blood samples for sulfonamide determinations were taken, in most instances at the following intervals after treatment was started: two, four, six, eight, twelve, twenty and twenty-four hours. In some instances, when indicated, a second or even a third hypodermoclysis was given. As a rule it was possible to give the drugs orally after the patient had received from 5 to 20 Gm. of the sulfonamide compound subcutaneously. All blood concentrations were done by the method of Bratton and Marshall.[2]

BLOOD CONCENTRATION CURVES FOLLOWING HYPODERMIC ADMINISTRATION

The trend of blood concentrations after hypodermic administration of three sulfonamide compounds is illustrated in the charts. The cases selected were chosen because they illustrate the variations encountered and show the limits within which most of the curves fall.

The patients employed in this investigation were all hospitalized, and sulfonamide therapy was indicated for all of them. Most of the patients had pneumococcic pneumonia. Kidney function, as judged by urinalysis and by determinations of the blood nonprotein nitrogen, was normal in most instances. The average intake was 3,000 cc. in twenty-four hours.

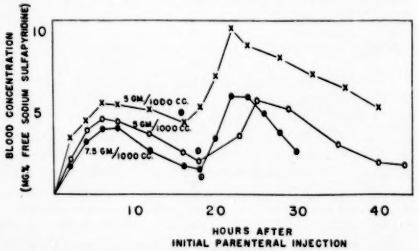

Chart 1.—The blood concentration curves following the parenteral administration of sodium sulfapyridine to 3 patients. The 2 patients whose curves are indicated by solid dots and hollow dots received an initial hypodermoclysis of 7.5 Gm. and 5 Gm. respectively of sodium sulfapyridine in 1,000 cc. of saline solution. The patient whose curve is indicated by X's received an initial intravenous injection of 2 Gm. of sodium sulfapyridine in 400 cc. of saline solution. Immediately thereafter a hypodermoclysis of 3 Gm. of sodium sulfapyridine in 600 cc. of saline solution was administered. At the points indicated by a circled plus sign a second hypodermoclysis of 1,000 cc. was given to each patient. The concentration of the second clysis was the same as that previously given.

When sulfapyridine was employed the maximum blood concentration was reached six hours after the first clysis was started (chart 1). This maximal value varied between 4 and 5.6 mg. per hundred cubic centimeters. No obvious relationship was apparent between the dosage and the type of blood concentration curve. The renal function was normal and the fluid intake and output were comparable for each of 3 patients. From twelve to sixteen hours after the first subcutaneous dose was started the blood concentration decreased rapidly. At the end of this interval a second clysis was started. The blood concentration curves following the second hypodermoclysis showed a summation, the second series of values being higher than the first, but they followed the same pattern.

Among the patients receiving sodium sulfathiazole the maximum concentration was attained in from five to eight hours after the first hypodermoclysis (chart 2).

2. Bratton, A. C., and Marshall, E. K., Jr.: New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128:** 537 (May) 1939.

Approximately the same interval elapsed before the maximum concentration was reached after the second subcutaneous injection. The highest concentrations varied between 3 and 12.4 mg. per hundred cubic centimeters. As in the group of patients treated with sulfapyridine, it was impossible to correlate accurately the

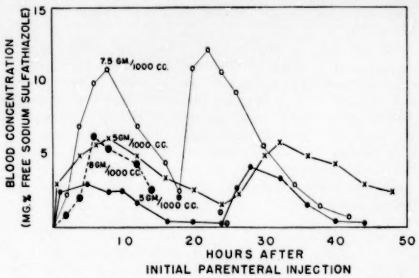

Chart 2.—The blood concentration curves after parenteral administration of sodium sulfathiazole to 4 patients. The 2 patients whose curves are indicated by X's and small solid dots received in initial intravenous dose of 1 Gm. of sodium sulfathiazole in 200 cc. of saline solution. This was followed immediately by a hypodermoclysis of 800 cc. of the same 0.5 per cent solution. The 2 patients whose curves are indicated by hollow dots and large solid dots received hypodermoclysis initially of 1,000 cc. of 0.75 per cent and 0.8 per cent sodium sulfathiazole in saline solution respectively. At the points indicated by a circled plus sign 3 patients received second hypodermoclyses of 1,000 cc. Each of the latter doses corresponded in strength to that previously administered to each patient.

blood concentration with the dosage, fluid balance and renal function. Likewise as in the group of sulfapyridine treated patients, the optimum time for a second hypodermoclysis was from twelve to sixteen hours after the first subcutaneous dose. The blood concentration curves after the second injection followed a pattern similar to that observed in patients treated with sulfapyridine.

The maximum concentrations of sulfadiazine in the blood after hypodermic injection varied from 4.5 to 16 mg. per hundred cubic centimeters (chart 3). These values were reached in from four to eight hours after the administration was started. The optimum time for giving the second hypodermoclysis was twenty to thirty hours after the first had been started. The results obtained in this group of patients also illustrate the

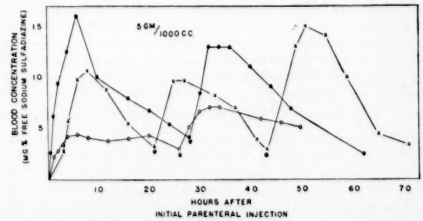

Chart 3.—The blood concentration curves after the parenteral administration of sodium sulfadiazine to 3 patients. Each of these patients received an initial intravenous dose of 200 cc. of 0.5 per cent sodium sulfadiazine in saline solution after which 800 cc. of the same solution was given as a hypodermoclysis. At the points indicated by a circled plus sign each patient received a second hypodermoclysis of 1,000 cc. of the 0.5 per cent sodium sulfadiazine solution. One patient received a third hypodermoclysis of the same strength and amount.

lack of correlation between dosage, renal function, fluid balance and the pattern of the blood concentration curve. The patient having the lowest blood concentration values had a blood nonprotein nitrogen of 83 mg. per

hundred cubic centimeters, while the patient showing the highest blood concentration had apparently normal renal function. In both cases the fluid intake and output were adequate and comparable. In most instances summation was noted in the curves for the second and third hypodermoclyses of sodium sulfadiazine, although there is little evidence of this in the curves selected for illustration in chart 3.

COMMENT

From the data presented it is apparent that there are wide variations in the blood concentration curves of different patients following the hypodermic administration of each of the sulfonamide solutions studied. Plummer and Wheeler [3] noted this unpredictable variation in the blood concentration of sodium sulfadiazine when repeated doses were given intravenously. Because of the decided variations in the blood concentrations of the sulfonamide compound attained in different patients following the subcutaneous injections of these drugs, one can neither adopt a standard dosage nor give subsequent doses at arbitrarily fixed intervals. If such a routine was followed 1 patient might receive a toxic dose while another might receive an inadequate one. In order to circumvent these difficulties it is necessary to guide treatment by following the blood concentrations at frequent intervals. By so doing one may determine the pattern of the blood concentration curve for each patient and give subsequent doses at an optimal time; also the dosage may be altered to suit the case in question.

An idea of the pattern of the blood concentration curve may be obtained by determining blood sulfonamide levels between four and eight hours and again between fourteen and eighteen hours after treatment has been started. Subsequent treatment may be guided by the use of these two determinations.

In general, it has been found necessary to give the following approximate amounts per thousand cubic centimeter hypodermoclysis to achieve adequate blood concentrations: sulfathiazole 7.5 to 8 Gm. (the blood concentrations may be low even with this dosage), sulfapyridine 5 to 7 Gm. and sulfadiazine 5 Gm. In general, the blood concentrations were higher and more prolonged after the use of sulfadiazine subcutaneously than after the use of the other sulfonamide compounds. This difference in the metabolism of sulfadiazine conforms to that noted by others.[4]

It is apparent that the intravenous doses given to several of the patients included here were too small to achieve an immediate high blood concentration. The intravenous doses in the amounts used caused little appreciable difference in the blood concentration curves as compared with those obtained following initial subcutaneous doses. Hence, if one desires to obtain an immediate high blood concentration, a larger intravenous dose must be given than was used in this study.

No attempt has been made in this study to evaluate the therapeutic effect of these drugs when given subcutaneously. However, the impression was gained that this route of administration gives results comparable to those achieved by oral administration.

This paper is not an attempt to promote the subcutaneous mode of administration when the drugs can be given orally. Most patients can and should be treated by the oral mode of administration. However, it is felt that giving the drugs by hypodermic injection is a great convenience and gives satisfactory results for patients who are unable to take the sulfonamides by mouth for one reason or another—such as an unfavorable mental state, persistent vomiting and sometimes after an operation.

CONCLUSION

1. The sodium salts of sulfapyridine, sulfathiazole and sulfadiazine may be conveniently and safely administered subcutaneously when the patient cannot take the drugs orally. The subcutaneous administration of the sodium sulfonamides to 160 patients caused no local reactions.

2. These drugs may be given subcutaneously in concentrations of from 0.4 per cent to 0.8 per cent in isotonic solution of three chlorides, isotonic solution of sodium chloride or one-sixth molar sodium lactate solution.

3. Decided variations in the blood concentrations of the sodium sulfonamides were encountered when given by hypodermoclysis. These values were not predictable. Treatment must therefore be based on the blood concentrations encountered for each individual patient.

4. Sodium sulfadiazine was the most convenient drug to use hypodermically. A 1,000 cc. hypodermoclysis containing 5 Gm. of this drug usually gave satisfactory blood concentrations for about twenty hours.

3. Wheeler, Charles, and Plummer, Norman: Sulfadiazine and Sodium Sulfadiazine: A Comparison of Certain of Their Clinical and Pharmacologic Values, Ann. Int. Med. **16**: 269 (Feb.) 1942.

4. Reinhold, J. G.; Flippin, H. F.; Schwartz, Leon, and Domm, A. H.: The Absorption, Distribution and Excretion of 2-Sulfanilamido-Pyrimidine (Sulfapyrimidine, Sulfadiazine), Am. J. M. Sc. **201**: 106-115 (Jan.) 1941. Peterson, O. L.; Strauss, Elias; Taylor, F. H., and Finland, Maxwell: The Absorption, Excretion, and Distribution of Sulfadiazine (2-Sulfanilamido-Pyrimidine), ibid. **201**: 357 (March) 1941.

AN OUTBREAK OF STREPTOCOCCIC SEPTIC SORE THROAT IN AN ARMY CAMP

CLINICAL AND EPIDEMIOLOGIC OBSERVATIONS

ARTHUR L. BLOOMFIELD, M.D.
AND
LOWELL A. RANTZ, M.D.
Consultants to the Secretary of War
SAN FRANCISCO

This report of an outbreak of streptococcic sore throat in an army camp is made because there were clinical and epidemiologic features of unusual interest.

BACKGROUND

The outbreak occurred on June 17, 1942 and the next succeeding few days in a Western army camp. The camp is an assembly center for troops coming from various parts of the country. It is situated in a flat area; the weather is hot and dry in June, and ordinarily there is no streptococcic sore throat during this season. At the time of the outbreak the camp was still partly under construction.

THE OUTBREAK

The outbreak began with explosive suddenness at a time when there was no illness in the camp. There were, however, a number of men who had had "tonsillitis" at other establishments within the past few weeks before coming to this camp. The number of men reporting sick each day is shown in table 1.

All the cases occurred in the personnel of a single unit (area 1) of some 3,000 men. Thus the incidence was approximately 10 per cent. However, it is not cer-

Lieutenant Colonel Culpepper and other medical officers gave the authors assistance and advice.

This investigation was aided through the Commission on Hemolytic Streptococcal Infections, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, United States Army.

tain that all the members of the unit were exposed, so that the exact morbidity in relation to ingestion of streptococci is not known.

GROSS EPIDEMIOLOGIC FEATURES

The explosiveness of the outbreak with the great number of cases on the first day without reports of sore throats during the preceding week suggested ingestion

TABLE 1.—*Incidence of Cases*

Date	Number of Cases
June 17	135
18	156
19	37
20	5
21	8
Total	341

TABLE 2.—*Complications*

Total patients		341
Peritonsillar abscess		18
Incised	2	
Rupture	2	
Spontaneous resolution	14	
Otitis media		7
Incised	0	
Rupture	1	

of streptococci in large numbers. The fact that each area has its own kitchen and mess halls and that the men were all from one area is in harmony with this idea. However, milk, which is the commonest vehicle for infection in outbreaks of this sort, seemed to be ruled out, since it was obtained in individual pasteurized half-pint bottles from a high class dairy. No other article of food could be positively incriminated, but it was our impression that some dish which a large number of men ate had become highly contaminated with hemolytic streptococci.

There was no evidence of spread of the infection from person to person. Not a single case occurred among the medical officers or hospital personnel even though they were intensively exposed and were unable to use the usual isolation precautions because the hospital was not yet fully equipped at the time of the outbreak. It seems probable that the streptococci causing the outbreak were relatively "avirulent" and produced disease only because they were ingested in huge numbers. Further evidence to this effect will be presented later.

CLINICAL FEATURES

The men came down abruptly with sore throat and malaise and in the more severe cases with chills and high fever. On the whole, very few of the patients seemed dangerously ill, and there were no deaths. The appearance of the throat was typical of acute streptococcic tonsillitis. The tonsils were swollen, in some cases to huge proportions, and they were stippled with white patches of exudate. In those whose tonsils had been removed there was inflammation of the bits of lymphadenoid tissue in the pharynx and tonsillar fossae. In approximately one fourth of the cases there was a classic scarlatinal rash which ran the usual course, with eventual desquamation of the glove type. In other patients there were only traces of the exanthem, and in the majority a rash was not seen at any time. After a few days of fever, sore throat resolved and general symptoms quickly cleared. Aside from a few insignificant local lesions to be mentioned presently there were none of the usual complications of outbreaks of septic sore throat—no general sepsis, suppurative adenitis or peritonitis.

COMPLICATIONS

As already stated, there were no deaths or serious septic complications. The medical officers at the camp furnished the data given in table 2.

These figures were supplemented by our own study of 127 men. Among them there was 1 who gave a story of "abscess in the throat" bursting during the acute attack but with no further trouble. Two men said that about a week after onset they had a running ear (not opened), but there was no drainage at the time of our examination two weeks later.

To sum it up, then, there were to all intents and purposes no septic complications in this outbreak. Whether this unusual state of affairs was due to sulfonamide therapy or to infection with an organism of "low virulence" is not clear.

TABLE 3.—*Arthralgic Symptoms in Convalescents*

Series No.	Severity of Original Attack	Symptoms	Objective Findings July 9	Condition of Throat July 9
110	Moderate	About a week after onset had vague aches and pains—fairly bad—lasted 3 days	None	Throat clear
48	Severe	About a week after onset "relapse" with a little fever; left knee hurt for 1 day	None	Throat clear; small tonsil
98	Mild	Headache and pain in back ever since onset; left knee hurt for 1 day	None	Throat clear; tonsils out
4	Moderate	Well for a week—then back ached for 2 days; feels well again now	None	Small clean tonsils; large glands at angles of jaws
38	Mild	A little pain in left knee today	None	Throat clean; small tonsils
93	Severe	About 1 week ago right elbow was sore for a day; not since, and all right now	None	Large congested tonsils
10	Moderate	Feels stiff and tired each morning	None	Throat clear
112	Mild	Well until today; this morning nausea, malaise, and knees ache; temperature subnormal	None	Throat clear; tonsils small and clean
118	Severe	Feels tired; has no energy; has aching through back	None	Tonsils out
135	Severe	Aching of lower part of back since onset—not bad	None	Large clean tonsils
125	Severe	Felt fairly well until today; this morning had temperature of 100 F. and has pain in neck and over eyes	None	Huge congested tonsils
109	Moderate	A few days ago both wrists were sore for 2 days; well now	None	Large congested tonsils
114	Mild	Muscles around left knee have been sore	None	Throat clear
21	Mild	Has "ached all over" ever since onset; not specially in joints	None	Throat clear

SEQUELAE

An outbreak of this sort under highly uniform conditions seemed to offer an especially good opportunity for the study of sequelae. We interviewed and examined 127 men on July 9, twenty-two days after onset.

Septic Sequelae.—There were no late septic complications.

Adenitis.—There were no instances of general adenitis, although a good many of the men still had

enlarged glands at the angle of the jaw, probably associated with persisting tonsillar infection.

Arthritis, Arthralgia and Rheumatic Fever.—The view is widely held that rheumatic fever may be "activated" by acute hemolytic streptococcic infection.[1] Some observers, however, are not certain that the arthralgia or mild arthritis which often is noted about three weeks after an attack of septic sore throat is true rheumatic fever. It is not our purpose to enter into this discussion now; we shall merely report findings. Fourteen men, or 11 per cent of those interrogated, gave a story of mild symptoms which perhaps fall into this group. The details are given in table 3. It is seen that disability was slight and that there were no objective findings in any case at the time of our examination. So that, while the significance of these phenomena is not entirely clear, we are not inclined to interpret them as rheumatic fever but rather to class them with the mild aches and pains which are noted during convalescence from any acute infectious disease and which are not followed by further trouble.

Blood Pressure.—The readings were made with the subject sitting. With a very few exceptions the men were still in the hospital although ambulatory. The temperature of the room was high and the humidity low. The conditions were such as to promote low rather than high blood pressure. We had no previous control observations. Whenever the reading seemed high it was carefully checked. The results are given in table 4. One gets the impression that there are more men with slight hypertension than one would expect in a group of this sort.

The Urine.—Here was an unusual opportunity to make careful studies of urinary sediment in a large group of young men who had been subjected simultaneously to a highly specific type of streptococcic infection. Through the cooperation of the medical officers it was possible to collect 59 specimens, which were concentrated according to the specifications of Addis.[2] Specimens of urine were obtained as well from most of the other men in the group. We are indebted to Dr. Thomas Addis for personally examining many of these. It may be said that the quantitative studies of the urinary sediment were conspicuously negative. In no case were there any findings to suggest the presence of nephritis. The few hyaline and granular casts, the occasional red blood cells and white and epithelial cells were within the normal limits laid down by Addis.[2] In case 48 there was a slight proteinuria which we had no chance to investigate further. This outbreak was followed by no case of clinical nephritis and three weeks after onset there were no urinary findings to indicate renal injury. This is not entirely in accord with the observations of Lyttle[3] but agrees with our previous experience that, whereas acute nephritis is often preceded by streptococcic sore throat, only an occasional case of septic sore throat is followed by nephritis.

The Local Condition of the Throat.—Following a streptococcic septic sore throat it is often observed that the tonsils remain large and have a succulent congested appearance for a considerable time before they shrink to their previous proportions. At the time of our investigation 29, or 23 per cent, of the group examined still had tonsils which were definitely congested and obviously had not returned to their usual state, although only 2 men complained of dryness and irritation on swallowing.

Convalescence and General Well-Being.—Tonsillitis is usually considered a mild disease which entails no great disability. The men in this study were carefully interrogated three weeks after onset as to their general strength and well-being. Ninety, or 71 + per cent, still felt below par generally, tired easily and did not consider themselves ready for duty. Seven, or 5.5 per cent, were definitely unwell, with great fatigue on slight effort, definite lack of well-being or vague aches and pains. No significant difference was noted between men who had had a rash ("scarlet fever") and those without rash. It is clear, then, that after any variety of streptococcic septic sore throat full recovery in the sense of restoration of physical fitness may often take more than three weeks, a fact which we do not believe is fully appreciated by physicians.

BACTERIOLOGIC FINDINGS AND CLINICAL INTERPRETATION

Throat cultures taken on June 20 at the height of the outbreak from a generous random sample of sick men including patients both with and without rash in various wards all showed group A hemolytic streptococci in large numbers. These turned out in every case to be of the same Griffith subtype, namely type 15. This furnishes final proof of a single source of infection, especially as this type has been uncommon in the region and was found by Rantz[4] only seven times among 260 strains.

TABLE 4.—*Blood Pressure Readings of One Hundred and Twenty-Seven Men*

Systolic			Diastolic		
Blood Pressure, Mm. Hg	Number of Men	Per Cent	Blood Pressure, Mm. Hg	Number of Men	Per Cent
Up to 100	9	7.3	Up to 60	7	5.5
101-110	34	27.0	61- 70	32	25.2
111-120	42	33.0	71- 80	50	39.3
121-130	19	15.0	81- 90	27	21.2
131-140	16	12.5	81-100	9	7.3
141+	7*	5.5	101-110	2†	1.5
	127			127	

* 142/80; 150/80; 150/80; 150/90; 150/90; 150/92; 170/110.
† 170/110; 140/105.

At this point a digression on the clinical interpretation of the cases with and without scarlatinal rash is necessary, since there is still confusion in the minds of some as to this matter. Briefly, both clinical "tonsillitis"[5] and clinical "scarlet fever"[6] are now known to be specific hemolytic streptococcus infections of the tonsils and lymphadenoid tissue in the pharynx. Certain strains of streptococci produce a soluble toxin[7] which in nonimmune people causes the scarlatinal rash. Absorption of this "rash toxin" is followed by antitoxic immunity to its effects;[8] hence if a person who has had

1. Coburn, A. F.: The Factor of Infection in the Rheumatic State, Baltimore, Williams & Wilkins Company, 1931. Mote, J. R., and Jones, T. D.: Studies of Hemolytic Streptococcal Antibodies, J. Immunol. **41**: 61, 87 (May) 1941.
2. Addis, Thomas: The Number of Formed Elements in the Urinary Sediment of Normal Individuals, J. Clin. Investigation **2**: 409 (June) 1926.
3. Lyttle, J. D.: The Addis Sediment Count in Scarlet Fever, J. Clin. Investigation **12**: 95 (Jan.) 1933.
4. Rantz, L. A.: The Serological Typing of Hemolytic Streptococci of the Lancefield Group A, J. Clin. Investigation **21**: 217 (March) 1942.
5. Bloomfield, A. L., and Felty, A. R.: Bacteriological Observations on Acute Tonsillitis with Reference to Epidemiology and Susceptibility, Arch. Int. Med. **32**: 483 (Oct.) 1923.
6. Dick, G. F., and Dick, Gladys H.: Experimental Scarlet Fever, J. A. M. A. **81**: 1166 (Oct. 6) 1923.
7. Dick, G. F., and Dick, Gladys H.: Scarlet Fever Toxin in Preventive Immunization, J. A. M. A. **82**: 544 (Feb. 16) 1924. Stock, A. H.: Further Purification and Concentration of Scarlet Fever Toxin, J. Biol. Chem. **142**: 777 (Feb.) 1942.
8. Davies, J. A.: Postscarlatinal Immunity in Patients Treated with Antitoxin, J. Clin. Investigation **3**: 423 (June) 1926.

"scarlet fever" is later reinfected with the same organism he may have no rash but only what is ordinarily called tonsillitis.[9] These relations, which explain the paradox of permanent immunity following one attack of "scarlet fever" with susceptibility of the same person to frequent attacks of "tonsillitis," are diagrammed in table 5.

One may raise the question of whether the use of the term "scarlet fever" with the implication of a fundamental difference from acute "tonsillitis" does not serve to maintain confusion and diagnostic quibbling. The entire group should perhaps be referred to as streptococcic septic sore throat (with or without associated scarlatinal rash), and the same rules for isolation and quarantine should hold for all. Health departments that quarantine "scarlet fever" but not "tonsillitis" show complete lack of understanding of the subject.

This position was fully supported by the present study. Among 77 men of whom we had a definite record, 52 had no rash and 25 did have a rash. Eleven among the 77 gave a history of scarlet fever in the past; they were all in the group who had no rash now. Statistical analysis shows only about one chance in a hundred of this finding not being significant. Furthermore, since the same strain of streptococcus was responsible for all the cases, it is clear that absence of

TABLE 5.—*Diagram of Immune Status of Persons to Infecting Streptococcus*

Infecting Streptococcus	Immune Status of Infected Person	Clinical Result
Produces rash toxin in the patient	Nonimmune to rash toxin	"Scarlet fever"
	Immune to rash toxin	"Tonsillitis"
Does not produce rash toxin in the patient	Nonimmune to rash toxin	"Tonsillitis"
	Immune to rash toxin	"Tonsillitis"

rash must be explained by immunity to "rash toxin," unless one assumes that the organisms unaccountably failed to produce erythrogenic toxin in certain persons.

Finally, there was no relation between presence or absence of rash and severity of the disease or incidence of complications. This is an important observation, since the question of whether the so-called scarlet fever toxin produces clinical effects other than the rash and whether antitoxin does more than neutralize the rash has never been finally settled. The Dicks, in the early days of the subject,[6] pointed out that their toxin when injected into susceptible human beings produced not only rash but nausea, vomiting, malaise and fever as well. Trask,[10] on the other hand, showed that the clinical severity of the attack did not parallel the amount of "toxin" in the blood serum; finally, the highly purified "erythrogenic" toxin recently isolated by Stock and his associates [11] by electrophoretic methods in such concentrations that there were 100 to 150 million skin test doses per milligram of the material has not been yet tried out for systemic effects.

At any rate, there was no clinical indication in the present outbreak that the patients with rash were suffering from any other symptoms not equally present in the men without rash.

9. For literature on this point see Bloomfield, A. L.: The Association of Susceptibility to Scarlet Fever and Acute Tonsillitis, California & West. Med. **28**: 477 (April) 1928.

10. Trask, J. D.: The Amount of Scarlatinal Toxin in the Blood of Patients with Scarlet Fever, J. Clin. Investigation **3**: 391 (June) 1926.

11. Krejci, L. E.; Stock, A. H.; Sanigar, E. B., and Kraemer, E. O.: The Electrophoretic Isolation of Erythrogenic Toxin of Scarlet Fever and the Determination of Its Chemical and Physical Properties, J. Biol. Chem. **142**: 785 (Feb.) 1942.

RELATION OF TONSILS TO INCIDENCE OF SEPTIC SORE THROAT

It is well known that tonsillectomy confers a high degree of protection against acute streptococcic septic sore throat. Bloomfield and Felty [5] found in the case of an institutional group of 179 persons that among 77 without tonsils 6, or 7.8 per cent, had septic sore throat whereas during the same season among 102 whose tonsils had not been removed 27, or 26.5 per cent, had attacks. Only 6 of 33 cases, or 18 per cent, occurred in persons who had had a tonsillectomy. In the present outbreak we unfortunately have no data on the number in the whole unit with and without tonsils. However, among a group of 127 men whom we examined the condition occurred in only 20, or 16 per cent, who had had a tonsillectomy.

PERSISTENCE OF STREPTOCOCCI IN TONSILS DURING CONVALESCENCE IN RELATION TO CASES

During the acute stages of septic sore throat hemolytic streptococci are obtained in huge numbers from the surface of the tonsils and pharynx. In convalescence fewer colonies are isolated from the pharynx, although many can still be recovered from the surface of the tonsils. After a variable number of weeks, surface swabs may no longer yield any hemolytic streptococci, but cultures of material aspirated from tonsillar cysts show that the organisms persist in the depths of the lymphadenoid tissue.[5]

On July 9, approximately three weeks after onset and just before discharge, we took cultures from 36 convalescents. Of these, 19, or 53 per cent, yielded hemolytic streptococci from surface swabs. In every case but 1 the organisms were of the same type (Griffith type 15) as those obtained during the acute stage of the disease. The 1 exception was a type 8. It can be concluded, therefore, that when the convalescents were discharged to barracks approximately one half were carriers. In spite of contact with the other men only 1 further case of septic sore throat was reported, on July 7. A culture taken from this man yielded hemolytic streptococci (Griffith type 15), so that he was undoubtedly a "return" case.

A good deal of work has been done recently on the Griffith subtyping of streptococci recovered from the same patient during the acute stages of septic sore throat and later on during convalescence. Some workers have found striking changes in the streptococcic flora of the throat almost from day to day.[12] Furthermore, it has been pointed out that the complications or sequelae which occur in the second or third week after scarlet fever or septic sore throat often seem to be due to a streptococcus of different type from that originally isolated during the acute attack.[13] Some of the work that has been reported is open to criticism on technical grounds, but in the main it is probably correct. It is therefore of note that in the present outbreak cultures made after three weeks showed either the original type of streptococcus (Griffith type 15), with the exception of 1 case, or no hemolytic streptococci at all. The question may be raised (but cannot be answered now) whether the absence of secondary infection with other types of streptococci is to be correlated with the lack of complications in our group.

12. de Waal, H. L.: The Serological Types of Hemolytic Streptococci in Relation to the Epidemiology of Scarlet Fever and Its Complications, J. Hyg. **40**: 172 (March) 1940.

13. Allison, V. D., and Brown, W. A.: Reinfection as a Cause of Complications and Relapses in Scarlet Fever Wards, J. Hyg. **37**: 153 (April) 1937.

It is of great interest that the introduction of large numbers of convalescent carriers into the uninfected group was not followed by more "return" cases, but this is exactly what one would expect on the basis of knowledge of "normal" hemolytic streptococcus parasitism in the throats of healthy persons. It has been shown, first, that under ordinary conditions a person does not become a contact carrier without going through a clinical attack of tonsillitis,[14] and second, that acquisition of disease from a convalescent carrier, again under ordinary conditions of parasitism, occurs only if there is a very high degree of intimate contact.[15] Furthermore, to be infected the person will usually not be a carrier and he must have a low natural resistance to hemolytic streptococcus infection.[5] These considerations are of course altered under conditions of true epidemic spread of streptococci such as occurred in the Army camps in 1918 following measles and influenza.

We are now in a position to interpret the present outbreak. It was clearly not an epidemic in the sense of disease occurring by spread from man to man but rather a mass infection of the entire group from a common source. The failure of contacts to acquire sore throat suggests that the organism was not highly "virulent" and that infection was the result of ingestion of huge doses of organisms. This view is finally confirmed by the fact that when large numbers of convalescent carriers were returned into the general group only 1 case of septic sore throat resulted. In other words, a "normal" state of streptococcic parasitism existed of such a sort that intensive contact with carriers would have been necessary before further disease could be produced. There was no tendency to those obscure upsets of immunologic balance which lead to epidemic spread of streptococci through a group by person to person passage with high incidence of infection.

THERAPY AND EFFECTS

Treatment consisted of rest in bed, general measures and the sulfonamides. We are unable to draw definite conclusions as to the efficacy of the sulfonamide therapy. Whether the extraordinary lack of complications and the generally mild course of the disease is to be attributed to the drugs cannot be stated.[16] It should be noted, however, that the sulfonamides have not been found by others to be highly effective in this type of streptococcic infection.[17]

CONCLUSIONS

1. A violent outbreak of septic sore throat which occurred in an Army camp was shown to be due to mass infection with hemolytic streptococcus Griffith type 15, a rare organism in the locality in which it occurred.

2. The contaminated article of food was not determined, but milk seemed ruled out as a source of infection.

3. An unusual feature of such a violent outbreak was the absence of complications. There were no deaths.

4. Sulfonamide therapy may have played a part in producing the mild clinical course.

5. From the epidemiologic standpoint it was shown that this outbreak was a mass infection occurring on a background of normal hemolytic streptococcus parasitism, which remained essentially undisturbed.

2398 Sacramento Street.

14. Bloomfield, A. L., and Felty, A. R.: Definition of Hemolytic Streptococcus Parasitism in the Upper Air Passages of Healthy People, Arch. Int. Med. **32**: 386 (Sept.) 1923.

15. Bloomfield, A. L., and Felty, A. R.: On the Mode of Spread of an Outbreak of Acute Tonsillitis, Bull. Johns Hopkins Hosp. **34**: 393 (Nov.) 1923.

16. Sako, Wallace; Dwan, P. F., and Platou, E. S.: Sulfanilamide and Serum in the Treatment of Prophylaxis of Scarlet Fever, J. A. M. A. **111**: 995 (Sept. 10) 1938.

17. For discussion see Top, F. H., and Young, O. C.: The Treatment of Moderately Severe Scarlet Fever, J. A. M. A. **117**: 2056 (Dec. 13) 1941.

A MILK BORNE EPIDEMIC OF BRUCELLOSIS

CAUSED BY THE PORCINE TYPE OF BRUCELLA (BRUCELLA SUIS) IN A RAW MILK SUPPLY

I. H. BORTS, M.D.
Associate Director, State Hygienic Laboratory
IOWA CITY

D. M. HARRIS, M.D.
Medical Director, District Health Service No. 3
LE MARS, IOWA

M. F. JOYNT, M.D.
MARCUS, IOWA

J. R. JENNINGS, B.A.
Milk Sanitarian, State Department of Health
AND
CARL F. JORDAN, M.D.
Epidemiologist, State Department of Health
DES MOINES, IOWA

Brucellosis of man, or undulant fever, is nearly always of sporadic occurrence. Animals chiefly concerned in the spread of infection are the cow, the hog and the goat. Organisms ordinarily causing infectious (contagious) abortion in these animals are respectively the bovine (Brucella abortus), the porcine (Brucella suis) and the caprine (Brucella melitensis) strains of Brucella. Infection in the cow is also known as Bang's disease and in the hog as Traum's disease. Although the possibility of occurrence of infection traceable to the goat needs to be kept in mind, the bovine and porcine strains of Brucella are probably the main offenders in most areas of the United States.

Main modes of conveyance of brucellosis to man are (1) through direct contact with infected animals or their abortion products and (2) through use of raw dairy products from infected sources. Brucellosis may occur in epidemic form when raw milk is consumed from cattle infected with a porcine strain of Brucella or a highly virulent strain of the bovine variety.

In animal inoculation work at the State Hygienic Laboratory, wide variation has been noted in the virulence of brucella strains as isolated from animal and human sources. Difference in virulence may help to account for the varied number of cases which occur among persons using a contaminated raw milk supply or having special forms of contact with infected animals.

In 1929 Farbar and Mathews [1] reported a milk borne outbreak of brucellosis (26 cases) and found that infection was caused by Brucella abortus. The agglutination test for Bang's disease proved positive in 7 of 23 dairy cows. Brucella abortus was isolated from the milk of 3 of the cows. Huddleson identified the brucella strain as of bovine origin.

A milk borne epidemic, comprising 30 cases and caused by Brucella suis, occurred in Council Bluffs, Pottawattamie County, Iowa, in 1933; this outbreak was

1. Farbar, Marion E., and Mathews, Frank P.: An Epidemic of Undulant Fever with a Study of the Associated Milk Supply, Ann. Int. Med. **2**: 875-880 (March) 1929.

reported by Beattie and Rice.[2] Brucella suis was isolated from the milk of a reacting dairy cow and from the blood of 6 patients.

In 1934-1935 a brucellosis outbreak occurred in an institution of elderly persons in Connecticut. The report by Horning [3] states that 14 cases developed in a group of 305 inmates and 81 employees. Among 3 fatal cases, blood cultures of 2 and culture of an abscess of the third patient proved positive for Brucella suis. The institution had its own dairy herd and "also kept swine"; 9 of 32 hogs showed positive reaction to the agglutination test, and 7 more were classed as suspicious.

THE MARCUS OUTBREAK

During the latter part of August and through Sept. 8, 1941 the State Hygienic Laboratory of the Iowa State Department of Health reported a series of positive agglutination tests for brucellosis on blood serum specimens from a number of patients with residence in Marcus (population 1,200), Cherokee County, Iowa. Among the first 9 patients concerned, 1 had been in poor health for several years following nephrectomy for a kidney tumor, another had been in contact with farm animals preceding the onset of symptoms, and 4 of the remaining 7 were father and 3 children in the same family. The reporting of but 1 case of brucellosis in a small urban community would have reflected the usual sporadic incidence of this disease. The occurrence of multiple cases, and especially of 4 in the same family, made it certain that something extraordinary had happened, suggesting the possibility of a Brucella suis infection.

Investigation took place on September 10 in cooperation with the attending physician (co-author M. F. J.). Home visits were made to see the patients who had complained for several weeks of fever, headache, chills or chilliness, severe night sweats, loss of weight and strength, lassitude, pain and weakness in the legs and in some instances a rather severe cough. Only 1 of this group of patients had come in contact with farm animals, cows or hogs, during the months before illness. There was a common factor, however, in that all had been supplied with milk from a dairyman (the W. H. dairy) who delivered raw milk.

Control measures were instituted on September 10. Arrangements were made for four local dairymen, all of whom furnished raw milk, to have animals tested for evidence of infectious abortion. Pending the result of agglutination tests, all milk was to be pasteurized in a nearby pasteurizing plant, before delivery to the public. The owner of the W. H. dairy went out of business forthwith; to our knowledge no raw milk or cream from this dairy reached families of the community after September 10. Bang's disease reactors were not reported among other dairy herds which formed part of the milk supply of Marcus.

EXTENT AND EVIDENCES OF INFECTION

1. *Occurrence of Additional Active and Latent Cases.*—Although the vehicle of infection, the suspected milk supply, was removed on September 10, new cases of brucellosis continued to appear throughout the remaining months of 1941 and into March of 1942. During the period from Aug. 12, 1941 to March 6, 1942 (including findings of the school survey) the blood serum of 77 persons in the Marcus community, all of whom had used milk from the W. H. dairy, showed positive agglutination in diagnostic dilution against brucella antigen. The peak of the epidemic, based on the number of positive agglutination reports, was reached in October. Titers of 75 of the 77 individuals who showed positive agglutination in diagnostic dilutions were as follows: 1:40 (2), 1:80 (5), 1:160 (2), 1:320 (21), 1:640 (16), 1:1,280 (17), 1:2,560 (2).

2. *Agglutination Survey.*—In order to obtain additional information regarding the extent of infection in the general population and to reveal latent or subclinical as well as clinical cases, agglutination tests were carried out on the serum of 237 persons in the parochial and public schools. The survey was made on October 21 in cooperation with parents and school officials. Twelve individuals (5.3 per cent) showed positive agglutination reactions for brucellosis in dilutions of from 1:80 to 1:2,560. Several members of the school group with positive agglutination findings had been sick or indisposed for several days during preceding weeks; others gave no history of illness and were apparently in good health. The simultaneous occurrence of subclinical along with clinical cases has been reported in previous brucellosis surveys conducted in Iowa.[4]

3. *Skin Tests with Brucellergen.*—On November 10 intradermal tests with brucellergen made separately from Brucella suis and Brucella abortus, supplied through the courtesy of Dr. I. F. Huddleson, D. V. M., of Michigan State College, were carried out on 266 persons in the public and parochial schools. Positive reactions as observed after forty-eight hours consisted of a varying sized oval area of erythema, induration and edema, which diminished within seventy-two hours. Forty-eight (18.0 per cent) showed a positive test with brucellergen abortus and 61 (22.9 per cent) with brucellergen suis. Reactions were more pronounced with the porcine than with the bovine antigen. A severe reaction, characterized by local necrosis with sloughing of skin and subcutaneous tissue, was noted in 1 instance, that of a girl aged 17, whose serum was not examined for brucella agglutination but who was exposed to the contaminated milk supply.

4. *Opsonocytophagic Tests.*—Seventy-five persons in the school group furnished blood for the opsonocytophagic test. Although 48 (64 per cent) of the reactions were interpreted as strong or very strong, there was no apparent relationship between such findings and exposure to the contaminated milk supply.

DISTRIBUTION OF CASES

One or more members of 51 families gave evidence of infection as revealed by positive agglutination tests or clinical illness. Multiple cases occurred in 15 homes. In the total group of 77, males numbered 44, females 33. The age group 1-9 included 29, of whom 11 were under 5 years of age. Eighteen were in the age group 10-19 and 20 in the group 20-39. The youngest patient was 7 months, the oldest 71 years of age.

INCUBATION PERIOD

The fact that positive agglutination reactions continued to occur for several months following removal of the contaminated milk supply on September 10 is

2. Beattie, C. P., and Rice, Raymond M.: Undulant Fever Due to Brucella of the Porcine Type, J. A. M. A. **102**: 1670-1674 (May 19) 1934.

3. Horning, Benjamin G.: Outbreak of Undulant Fever Due to Brucella Suis, J. A. M. A. **105**: 1978-1979 (Dec. 14) 1935.

4. Jordan, Carl F.: Infection in the Epidemiology of Undulant Fever in the General Population and in Selected Groups in Iowa, J. Infect. Dis. **48**: 526-540 (June) 1931.

attributed to the insidious nature of brucellosis and to the long incubation period, which Hardy, Frant and Kroll [5] found to vary from a week to four months.

TREATMENT

Acute brucellosis is a febrile disease, requiring strict bed rest during the course of illness and for ten days to two weeks after the temperature has returned to normal. An ample bed rest period is probably the best assurance against extended illness, as recurrence, complications and chronicity are less frequent when this regimen is followed.

In recent years the sulfonamide drugs have been used with varying success in the treatment of brucellosis. In the Marcus epidemic these drugs were used very sparingly, owing chiefly to the fact that all patients showed some degree of secondary anemia. In most instances the secondary anemia was a prominent finding; therefore sulfonamide therapy was withheld to avoid the possibility of adding insult to injury.

All the patients received brucellin, as developed by Huddleson and produced by the Iowa State Hygienic Laboratory. This preparation, a culture filtrate of brucella organisms, was given intramuscularly at intervals of three to five days dependent on symptoms. Brucellin is given subcutaneously in amount calculated to produce fever of 102 F. or above within a short time following injection. In general, the initial injection was 0.1 cc. and the dosage increased or diminished to achieve the desired febrile reaction. Maximum dosage was 1 cc. These treatments were administered until the patient received 1 cc. of brucellin without febrile reaction. In most cases three repeated doses were given after the febrile reaction had ceased. The average number of injections was fifteen. After four treatments many of the patients had a temperature not exceeding 100 F. in spite of increased strength of injections. One patient had a total of thirty treatments before the desired afebrile condition was achieved.

COURSE

The average duration of fever was six to eight weeks. One patient was severely ill and bedfast for twelve weeks. There were no fatalities—all patients were reported (May 21, 1942) as having made satisfactory recovery.

SOURCE OF INFECTION

1. *Blood Culture Findings.*—In October and early November, blood cultures were obtained from 29 patients, specimens being incubated for a number of days, forwarded to the State Hygienic Laboratory and examined by one of us (I. H. B.). Of this number, Brucella suis was isolated from 13 or 45 per cent; had blood cultures been taken earlier in the course of the disease, a higher percentage of positives would have been expected. These findings confirmed the original conjecture that Brucella suis was the infecting agent. All the brucella strains isolated from this outbreak and identified as Brucella suis by the Huddleson method [6] were verified by the author of the method.

2. *Findings on the Dairy Farm.*— (*a*) Dairy Cows: Among 43 cows belonging to the W. H. Dairy, 4 reacting animals were encountered, 3 of which were definitely positive and a fourth one suspicious. Brucella suis was isolated from the milk of 2 of the reacting animals on direct culture of the gravity cream, using the Huddleson dye method and on blood and tryptose agar medium. On guinea pig inoculation Brucella suis was isolated from the cream of 3 of the reacting animals.

Lesions produced in guinea pigs inoculated with cream and with pure cultures isolated from the blood of ill patients at Marcus were mild in nature compared with lesions produced by other strains of Brucella suis previously isolated from similar sources. The laboratory and clinical findings suggest a Brucella suis strain of relatively low virulence. Whether virulence might have been reduced by residence in the cow's udder is a matter of speculation.

(*b*) Sows on the Farm: Inspection of the farm showed that hogs and dairy cows were allowed to mingle freely in the same lot. No history of frank abortion among sows was obtained, although the owner stated that about 20 young pigs, littered in the spring of 1941, were found dead after delivery, some living as long as a month. Blood tests on these animals, however, left no doubt as to their being infected. Twenty-four sows were tested, of which 11 showed positive and 3 suggestive agglutination reactions for infectious abortion.

COMMENT

1. In recent years articles by Alice Evans [7] and Simpson [8] have emphasized the importance of the blood culture and of repeated agglutination tests in the diagnosis of brucellosis, in particular the chronic form of this disease.

2. In spite of the apparent efficacy of brucellin when administered early in the course of illness, there are individuals who react with extreme elevation of temperature and exhaustion following the initial dosages. Three such patients in the Marcus outbreak were given sulfathiazole with satisfactory response and recovery.

3. On farms regarded as the source of infection of Brucella suis as isolated from the blood of patients, we have found it not unusual to fail to secure a history of abortion among hogs. This observation is in agreement with the following quotation from McNutt: [9] "Although abortion is one of the symptoms of Brucella suis infection in swine, it does not occur in the larger portion of cases." Agglutination tests are essential to the discovery of infectious abortion among hogs.

4. One of the patients in the Marcus outbreak, an expectant mother with one healthy child, acquired brucellosis in moderately severe form, being confirmed by a positive agglutination test. She aborted twin embryos during the fourth or fifth month of gestation; there was no other discernible cause for the abortion.

5. Among multiple cases which occurred in different homes during this epidemic, it is of interest to note that all 6 members of one family and, in another home, 6 of a family of 12, suffered an attack of brucellosis.

SUMMARY AND CONCLUSIONS

An epidemic of brucellosis included 77 persons who showed positive clinical or agglutination findings caused by the porcine strain of Brucella (Brucella suis) in a raw milk supply.

1. Isolation of Brucella from a blood culture stands first as a diagnostic aid in confirming the clinical diagnosis of brucellosis. Such isolation, moreover, when

5. Hardy, A. V.; Frant, Samuel, and Kroll, M. M.: The Incubation Period in Undulant Fever, J. Med. **19:** 408-412 (Oct.) 1938.

6. Huddleson, I. Forrest: Differentiation of the Species of the Genus Brucella, Am. J. Pub. Health (May 21) 1931.

7. Evans, Alice C.: Studies on Chronic Brucellosis, Pub. Health Rep. **52:** 1072-1077 (Aug. 6), 1419-1427 (Oct. 8) 1937. Evans, Alice C.; Robinson, Frank H., and Baumgartner, Leona, ibid. **53:** 1507-1525 (Aug. 26) 1938.

8. Simpson, Walter M.: The Diagnosis and Management of Brucellosis, Ann. Int. Med. **15:** 408-430 (Sept.) 1941.

9. McNutt, S. H.: Brucella Infection in Swine, Proc. 42d Ann. Meet. U. S. Live Stock Sanit. A. 1938, 1939, pp. 90-97; abstr. Bull. Hyg. **16:** 580 (Nov.) 1941.

supplemented by the Huddleson dye method, reveals the species of organism and is of great value in establishing the animal source of infection.

2. The agglutination test, repeated when negative, is second as a diagnostic aid to isolation of Brucella from the blood stream.

3. A positive intradermal test with brucellergen indicates recent or past exposure to brucella infection but "does not mean that the symptoms from which the patient is suffering at the time . . . are necessarily due to brucellosis" (Simpson [5]). The skin test is much less reliable than the agglutination test in diagnosis.

4. Careful pasteurization of all dairy products is an essential safeguard against milk borne brucellosis.

5. Hogs should not be permitted to run on the same lot with dairy cows.

6. Prevention of the occurrence of brucellosis in human beings requires a continuing program and effective measures for the eradication of infectious abortion among farm animals.

THE PREVENTION OF LIVER DAMAGE

AND THE FACILITATION OF REPAIR IN THE LIVER BY DIET

I. S. RAVDIN, M.D.
ELIZABETH THOROGOOD, A.B.
CECILIA RIEGEL, PH.D.
ROZANNE PETERS, A.B.
AND
J. E. RHOADS, M.D.
PHILADELPHIA

Although it is generally believed that attempts to improve the resistance of the liver to injury from hepatotoxic agents is a contribution of the present century, elaborate studies in this field were undertaken during the nineteenth century.[1] It was, however, the experiments of Opie and Alford [2] which led clinicians, at least in this country, to believe that a diet high in carbohydrate offered direct protection of the liver from the necrotizing effects of chloroform. Their work received confirmation in the later experiments of Davis, Hall and Whipple [3] and Graham.[4]

The unfortunate interpretation which clinicians placed on the results of these investigations led them to conclude that a high concentration of liver glycogen would in itself protect the liver from injury from a wide variety of agents, that the detoxifying power of the liver was proportional to its glycogen content and finally that hepatic regeneration would proceed more rapidly on a high carbohydrate diet than on any other.

In the early 1920's less and less emphasis came to be placed on the oral intake of foodstuffs in preparing the bad risk liver patient for operation and greater emphasis on the administration of intravenously injected dextrose. The rationale which led to this extension of therapy has been recently summarized by Soskin and Hyman.[5] Authors have repeatedly referred to the fact that larger amounts of dextrose could be deposited in the liver when the carbohydrate was administered intravenously than when equivalent amounts of carbohydrate were given orally (Banks and Sears [6]), although it rarely has been considered that larger amounts of foodstuffs can be given by the latter route than by the former.

It can be accepted as a fact that storage in important viscera will depend on a food intake sufficient to meet energy requirements on the one hand and to provide for food storage on the other. To believe that storage over any period of hours can take place when food intake falls below the needs for energy requirements is to disregard the fundamental laws governing metabolism. To perpetuate the statement that "cellular repair of the liver is best facilitated by a carbohydrate diet" [6] violates the fundamental knowledge available to us on cellular repair, for such repair in the main is dependent on protein components available to the regenerating tissue, and on a strictly carbohydrate diet repair would have to depend entirely on the breakdown of endogenous protein. Sanders and Garrison [7] have shown that the products of endogenous protein breakdown do not take the place of the protein in an adequate diet during wound repair.

In 1924 Moise and Smith [8] called attention to the fact that the diets used by the earlier investigators were neither pure (in the sense of consisting of single foodstuffs) nor adequate in amount for young growing dogs, which were the animals used by the investigators. In spite of this, many of us continued to place complete confidence in the carbohydrate diet as a means of protecting the liver from the assault of anesthesia and operation (Ravdin [9]).

It was better to provide in part for the energy requirements of the patient than to bring the patient to operation following a period of starvation. Where intravenous dextrose therapy reinforced oral feeding, the program accomplished a good deal and the morbidity and mortality of operations on many of the patients with serious liver dysfunction fell considerably.

In 1939 Goldschmidt, Vars and Ravdin [10] reported that maximum protection could not be afforded the liver against chloroform necrosis unless the diet was adequate in composition and amount, and administered for a sufficient time prior to exposure to the hepatotoxic agent. They concluded that a liver high in lipid content and high in available protein was maximally protected against injury.

Carbohydrate protected the liver from injury if, during the deposition of glycogen in the liver, fat was displaced, according to the hypothesis of Rosenfeld,[1] and if the ingested carbohydrate spared the body stores of protein. Protein, on the other hand, was found to be a much more active lipotropic agent than carbohydrate (Johnson, Ravdin, Vars and Zintel [11]) and, in addition, certain components of the protein molecule directly

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From the Harrison Department of Surgical Research, University of Pennsylvania School of Medicine, and the Surgical Service of the Hospital of the University of Pennsylvania.

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11. Johnson, Julian; Ravdin, I. S.; Vars, H. M., and Zintel, H. A.: Symposium on Preoperative and Postoperative Treatment: Effect of Diet on Composition of Liver in Presence of Obstruction of Common Bile Duct, Arch. Surg. **40**: 1104 (June) 1940.

protected the liver from the harmful effects of certain hepatotoxic agents. Messinger and Hawkins [12] found that a similar diet protected the liver from arsphenamine necrosis. Schultz [13] found it to protect against selenium injury, while M. I. Smith [14] reported that it protects against experimental sulfonamide hepatitis.

TABLE 1.—*Composition of Diet in Calories*

Carbohydrate	74 %
Protein	20 %
Fat	6 %

3,000 calories a day in three meals and three interval feedings

TABLE 2.—*The Relation of Obesity to Hepatic Fatty Acid*

Build	No. of Patients	Fatty Acid, Gm. per 100 Cc.
Average	31	3.9
Under normal	7	3.2
Obesity +	12	4.6
Obesity ++	21	6.4
Obesity +++	5	10.3±

A few years ago we found that approximately 29 per cent of patients with long standing gallstone disease had abnormally high amounts of lipid present in the liver. We have now studied the composition of the liver in 127 patients operated on for biliary tract disease. The operations were all done under local or spinal anesthesia. Some of the patients were not on a special diet prior to operation, while others were on a diet which we considered adequate in composition and amount for from five days to one month prior to operation.

The diet consisted of approximately 74 per cent of carbohydrate, 20 per cent of protein and not more than 6 per cent of fat. The carbohydrate was in large part obtained from the banana, for this foodstuff was found to be well tolerated by the patients. The protein in large part consisted of casein in the form of cottage cheese, skimmed milk and Casec. (A sample diet is given in table 1.) The diet must be varied in order to encourage the patient to eat a sufficient amount of food.

Only those patients were placed on a diet who gave evidence of long standing disease or serious interference with biliary function or who were jaundiced at the time of admission to the hospital. The patients operated on shortly after admission to the hospital did not appear to be ill or gave little or no evidence of serious hepatic injury.

This paper is based on the data obtained from 127 patients. Of these 37 were maintained for five days or more prior to operation on a diet adequate in composition and in caloric intake. In any consideration of diet it is important to select a diet which is adequate in the various constituents and which, at the same time, is sufficiently variable so that it will not become monotonous. It is important not only that the patients be offered a satisfactory diet but that they eat it. It cannot be too strongly pointed out that a high caloric intake is just as important as the composition of the food.

The patients we have had on a diet were all bad risk patients who had long standing biliary tract disease, usually with stones in the common duct, and many of them had been or were jaundiced at the time of admission to the hospital. Most of them were, in addition, moderately or decidedly obese, a factor which we have come to realize must be considered in deciding whether the patient should or should not be placed on a diet for some days prior to operation.

It was not always possible to get the patient to eat as much as we thought was necessary, and in such instances we have at times resorted to tube feeding, a method which is not used as frequently as it should be. In addition to the diet the patients received yeast, thiamine hydrochloride and one of the potent bile salt preparations. Such accessory therapy is, we believe, useful.

THE RELATION OF OBESITY TO HEPATIC FATTY ACID

An accurate record was kept of the build of 76 patients not on the diet. The data are given in table 2. It can be seen that increasing obesity is, as a rule, associated with an increasing concentration of hepatic lipid. It is interesting to note that the supposed inverse relationship between hepatic lipid and glycogen concentrations was not always present in these patients. Some of the highest hepatic glycogen concentrations were found in patients whose hepatic fatty acid concentrations were above 12 per cent. Conversely, some of the very low hepatic glycogen concentrations, 1 per cent or below, were found in patients with a normal fatty acid concentration. The reciprocal relationship between glycogen and fat described by Rosenfeld,[1] as a rule, was not found in these patients. No reliance, therefore, must be placed on the concentration of liver glycogen as an indicator of the lipid concentration.

THE RELATION OF HISTOLOGIC DIAGNOSIS TO HEPATIC FATTY ACID

We have come to know that the amount of fatty acids found by chemical analysis does not always closely parallel the amount found by histologic staining methods. It can be seen, however, from table 3 that the presence of large amounts of lipid as determined by staining methods does closely follow the chemical determinations.

TABLE 3.—*Microscopic Diagnosis of Fatty Infiltration*

	No. of Patients	Glycogen	Fatty Acid, Gm. per 100 Cc.
Mild fatty infiltration	18	2.8	4.6
Moderate fatty infiltration	31	3.5	5.4
Marked fatty infiltration	11	3.5	12.9

TABLE 4.—*Composition of the Liver*

	No. of Patients	Mean Glycogen, Gm. per 100 Cc.	Mean Fatty Acid, Gm per 100 Cc.
Patients not on diet	90	3.0	5.1
Patients with microscopically normal livers	16	2.8	4.1
Patients with severe disease not receiving the diet	10	3.2	14.2
Patients with severe disease receiving the diet	37	3.3	4.2

THE EFFECT OF DIET ON HEPATIC LIPID

In table 4 are given data which we believe demonstrate that an adequate diet, administered in sufficient amounts and for a long enough period, can condition

12. Messinger, W. J., and Hawkins, W. B.: Am. J. M. Sc. **199:** 216 (Feb.) 1940.
13. Schultz, Julius: Unpublished data.
14. Smith, M. I.; Lillie, R. D., and Stohlman, E. F.: Pub. Health Rep. **56:** 24 (Jan. 3) 1941.

a liver to minimal injury from a wide variety of hepatotoxic agents. The 37 patients who were on the diet had advanced biliary tract disease. The great majority of such patients without a period of preparation prior to operation run the risk of a variable degree of further degeneration or even necrosis subsequent to anesthetization and the trauma of operation.

The highest fatty acid concentration in the 37 patients on the diet was 7.4 Gm. per hundred cubic centimeters while the mean fatty acid concentration was 4.2 Gm. per hundred cubic centimeters. On the other hand, a group of 10 patients who were not so well prepared but who had comparable degrees of hepatic injury as determined by microscopic examinations had a mean fatty acid concentration of 14.2 Gm. per hundred cubic centimeters.

These data should be compared with those obtained from patients operated on for gallbladder disease but whose livers were reported as histologically normal. In these the hepatic fatty acid and glycogen concentrations were approximately the same as those which were obtained from the livers of patients with advanced hepatic histologic change but who had been on a diet for five or more days prior to operation.

The data demonstrate that one can by diet bring about a change in the liver so that the concentrations of glycogen and fatty acids are practically identical with those found in histologically normal livers. It is interesting to note that the mean concentration of glycogen in the last two groups was the same, while the mean fatty acid concentration varied by more than 300 per cent.

THE REGENERATION OF THE LIVER

It is generally agreed that hepatic regeneration takes place rapidly when circumstances favorable to regeneration are offered. For regeneration to proceed at a maximum rate it is necessary that the organism be offered foodstuffs which supply in maximum amount those components which must be utilized for cellular repair. Schultz and Vars [15] have found in the rat that repair is associated with a change in the ratio between the total liver protein and the nucleoprotein, the latter fraction increasing in amount during the period of repair. Such repair can be facilitated greatly if foodstuffs containing nuclear material are present in the diet during this period. Regardless of any other factors which may be involved, it has been found by them that the food best suited for facilitating this repair is liver itself.

During the past year we have placed our convalescing bad risk biliary tract patients on a diet which while similar in caloric intake and distributon to that used prior to operation, contains a generous share of the protein as liver. While it is difficult to evaluate such a procedure in man without further chemical and histologic data, we have been impressed with the smoothness of the convalescence of these patients and with the rapidity with which abnormalities of function which existed prior to operation have returned to normal thereafter. While casein is an active lipotropic agent and provides in maximal amounts those components of protein which provide protection from hepatotoxic agents, liver protein is more useful during periods when repair is desirable. Thus specificity in the protein provided during different phases of care receives additional significance.

15. Vars, H. M., and Schultz, Julius: Personal communication to the authors.

SUMMARY

1. The ingestion of carbohydrate alone does not afford maximal protection to the liver against a variety of hepatotoxic agents.

2. Glycogen cannot be accumulated in the liver over a considerable number of hours unless the individual is receiving a caloric intake in excess of his basal requirements.

3. Dextrose injected intravenously frequently fails to raise the liver glycogen because the total caloric requirement of the patient is not being provided.

4. Chemical analyses of liver biopsies showed striking correlation between the obesity of the patient and the lipid content of the liver.

5. Chemical analyses of the liver tissue of 37 patients obtained at operation indicates that a dietary regimen based on animal experimental work previously reported is effective in restoring the liver glycogen and liver lipid concentration of patients with severe microscopic damage to the values found in patients with simple cholecystic disease.

6. The average lipid content of severely damaged livers from 10 patients who were not prepared by diet was 14.2 per cent. The average lipid content of 37 patients who were prepared five days or longer with diet was 4.2 per cent. The glycogen content in the latter group was 3.3 per cent as compared with 2.8 per cent in a control group composed of specimens from 16 patients not receiving diet but with microscopically normal livers.

The diet employed consisted of at least 20 per cent protein, not over 6 per cent fat and 74 per cent carbohydrate. An adequate caloric intake is most important and was insisted on.

Before operation most of the protein content was in the form of casein. Following operation calf's liver is preferred on the basis of the experiments of Vars and Schultz,[15] which indicate that it facilitates the regeneration of liver tissue most effectively.

ABSTRACT OF DISCUSSION

DR. WALTER E. LEE, Philadelphia: This work, if confirmed, will mean the necessity for abandoning our faith in carbohydrates as the only agent to prepare patients with liver damage for surgery, the appreciation that, in addition, we must use protein, and that the ideal protein is liver tissue itself. The early work of Opie, Alfred, Davis and Hall and Whipple, which dates to 1914, and their conclusions that a high concentration of liver glycogen amply provided the necessary protection from a wide variety of agents, such as trauma, anesthesia and other toxic substances, was generally accepted, even by Ravdin, as late as 1929. In 1939 he first called attention to the fact that it was only when the liver was high in lipid content and available protein that its maximum protection against injury existed, and as a corollary that protein was far more active as a hepatotrophic agent than the carbohydrates. His suggestions as well as his experiments on animals and human beings are that this ideal diet which Drs. Ravdin and Rhoads have outlined is all right but it must be so palatable that the patients can eat it. Ravdin has found that, if it is not palatable and the patient refuses to take it, its need is so definite that it should be given by tube. As a result of their continued animal experiments and clinical work he is convinced that an adequate diet, as outlined in this paper, in sufficient amounts and given for a long enough time, will condition the liver against a large number of hepatotoxic agents and that when the liver is not so conditioned preoperatively there always exists the risk of liver damage in the form of degeneration and necrosis, as follow the routine anesthetic agents and operative trauma. Ravdin claims that patients when prepared by protein in addition to carbohydrate

will have but one third of the fatty acid concentration present, compared to those who are not so prepared; in other words, one third of those not prepared will have two thirds more fatty acid concentration. By taking tissue from the liver at the time of operation of patients who have been prepared with protein, they have found that it is quite possible to place the liver in a normal condition and that when they are not so prepared the figures already stated have been more or less constant. It would seem that he has demonstrated the fallacy of our depending entirely on the carbohydrate diet for the preoperative preparation of patients with damaged livers and he has made a constructive suggestion that by adding adequate protein to the carbohydrate diet it is possible preoperatively to place the liver of the patient in almost a normal condition.

TREATMENT OF BRONCHIAL ASTHMA

A SURVEY OF THE VALUE OF TREATMENT IN FOUR HUNDRED AND FIFTY-NINE CASES DURING TWENTY YEARS

LEON UNGER, M.D.
AND
A. ALVIN WOLF, M.D.
CHICAGO

The practice of allergy has developed into a major medical science within the past twenty years. It now seems advisable to analyze the results obtained in the treatment of the most important allergic condition, bronchial asthma.

This survey is divided into two parts. The first deals with the condition at this time in 207 cases previously reported.[1] The second concerns an additional 252 cases. No case was included unless the period of at least one year had elapsed since treatment was started, and this period of observation ranged up to twenty years. Cases from private practice were utilized in both studies because the cooperation of this group is greatly superior to and the information obtained much more reliable than that which can be secured in the clinic.

METHODS OF INVESTIGATION

Every effort was made to obtain correct information. With patients no longer under treatment, the data were usually secured by a questionnaire (fig. 1), with a return self addressed, stamped envelop; this brought in a fairly large number of answers, but in some cases a follow-up letter was more successful. Personal telephone calls were sometimes necessary, and, in a number of instances, the physician who had referred the patient was able to comment on the present status. A summarizing card (fig. 2) was made out for each patient and those still under observation or treatment had the card filled out directly from the history chart.

DIAGNOSIS OF BRONCHIAL ASTHMA

By means of a careful history and physical examination, all patients in the two groups were definitely diagnosed as suffering from bronchial asthma. Scratch tests were made at first, and, in cases in which sufficient information was not secured, intracutaneous tests followed. Ophthalmic and nasal tests and passive transfer tests were carried out when indicated. Clinical experiments with suspected allergens were made whenever possible and constitute our most authentic method of obtaining accurate information.

In addition, complete blood counts, urinalyses and Wassermann or Kahn tests were routinely done, and the sputum was examined both for tuberculosis and for eosinophils. Most of the patients were examined with a fluoroscope and chest films were also taken in suspicious cases. Other laboratory tests, e. g. electrocardiograms, basal metabolic readings and studies of the blood chemistry, were made in many of the cases.

In the course of the investigation, many patients, for various reasons, were not included. In some, the diagnosis of bronchial asthma was in doubt. Those with silicosis, tuberculosis or definite cardiac disease were excluded even though true bronchial asthma may have coexisted. Patients who cooperated poorly also were not included in the study, and in a fairly large number of instances the present condition of the patient could not be discovered.

METHODS OF TREATMENT

The treatment, whenever possible, is that based on the concept of allergy, namely elimination of the offending cause or causes, with great emphasis on the strictness of such elimination. This alone was sufficient in a number of cases. Hyposensitization, or desensitization, was carried out of those patients sensitive to allergens which cannot be completely avoided. These include such inhalant substances as pollen, molds, house dust, orris root, horse dander, feathers and cottonseed. Eggs, wheat and milk are so essential as also to deserve efforts at desensitization, either by the oral or by the hypodermic method.

But, when elimination and desensitization were unsuccessful, or in cases in which the causative factor could not be discovered, we were forced to use various nonspecific measures. These are many and varied, and time will permit only brief mention of a few. Epinephrine or aminophylline usually gives more or less relief from attacks. Other valuable drugs are ephedrine, the iodides, apomorphine, dextrose intravenously, and ether by rectum or by inhalation. Vaccines, stock or autogenous, are often very helpful but probably act nonspecifically. Roentgen therapy, oxygen and helium, hyperpyrexia, instillation of iodized oil in the bronchi, bronchoscopic aspiration, surgery of the nose and sinuses and other procedures all have their advocates in selected cases. In one's enthusiasm for the allergic methods of treatment one must not overlook general hygienic measures.

More detailed observations on various methods of treatment will be found in such textbooks as that of Tuft;[2] they have also been dealt with in various papers.[3]

RESULTS OF TREATMENT

Follow-Up of Cases Previously Reported.—In 1935, one of us (L. U.) reported on the results of treatment in a series of 207 patients with bronchial asthma who were under observation for a period of one to thirteen

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2. Tuft, Louis: Clinical Allergy, Philadelphia, W. B. Saunders Company, 1937.

3. Unger, Leon: Food Desensitization in Bronchial Asthma, Illinois M. J. **44**: 40 (July) 1923; Clinical Investigations in Allergy, J. Lab. & Clin. Med. **12**: 1159 (Sept.) 1927; Prognosis and Treatment of Bronchial Asthma, with Special Reference to Pediatrics, Illinois M. J. **58**: 270 (Oct.) 1930; Preventive Treatment of Bronchial Asthma and Hay Fever, Ann. Int. Med. **4**: 1328 (April) 1931; The Heart in Bronchial Asthma, J. Allergy **2**: 17 (Nov.) 1930; Treatment of Bronchial Asthma, South. M. J. **28**: 35 (Jan.) 1935; Paroxysmal Dyspnea: Diagnosis and Treatment, Illinois M. J. **68**: 268 (Sept.) 1935; The Use of Sulfonamide Drugs in Bronchial Asthma, J. Allergy **12**: 528 (Sept.) 1941.

years.[1] We now wish to discuss these same 207 patients with reference to their condition during the past seven years.

Table 1 shows the results of treatment in 1942 as compared to those in 1935. It can readily be seen that the percentages of those who obtained 100 per cent relief from symptoms for over a year or more were approximately the same. Likewise, the percentages of those who obtained 25 to 95 per cent relief were almost the same. The number of patients who received no benefit was less in 1942 than in 1935, chiefly because the number of deaths, many of which were not due to asthma, had increased during this period of seven years.

You were under my care for Asthma in _____

As a part of an intensive study of Asthma, it becomes important to know what has become of you. I would appreciate it if you would answer the following questions as accurately as you can:

1. If you are cured, when did the Asthma leave you? _____

2. Have you had any Asthma since I last saw you on _____?
If so, how much trouble (mild, moderate, severe)? What time of year ?
Have you had to take inhalations or injections of adrenalin; of so, how often _____?
Are you exposed to animals; if so, kind _____?
Do you sleep on feather pillows? Rubber covered ?

3. Have you taken or are you taking treatment for your Asthma from some other physician _____? If so, what sort of treatment _____?
What results _____?
Have you had any surgical operation for Asthma _____?
If so, what kind and what results _____?

4. Have you, at any time, changed climate because of Asthma _____?
If so, for how long, where did you go and what were the results _____?

In any case, I am anxious to know about you and I ask that you write any additional information about yourself and your Asthma on the back of this letter. All this will be of great service to those who suffer from Asthma. I would appreciate it if you would return this letter and answers promptly to me in the enclosed stamped envelope.

What is your present address?

Yours sincerely,

Fig. 1.—Questionnaire employed in this study.

CLINICAL CLASSIFICATION

Name: Age of Onset Sex Age First Seen
Address Occupation Source Last Seen

HISTORY
I Attacks
Cause Onset
Course
Season
Duration
Frequency
Cause of attacks
Relieved by
Other
II Between Attacks
Dyspnoea
Cough
Expectoration
Other
Environmental factors
Occupational factors
Food idiosyncrasies
Drug idiosyncrasies
Previous tests and results
Previous treatment
Change of climate
Family History
Past History

EXAMINATION Wt. B.P.
Type
Chest deformities
Cyanosis
Lungs
Wheezing
Prolonged exp.
Emphysema
Heart
Other findings
X-ray chest
Eosinophilia
Blood
Sputum
Skin Tests
Cutaneous
Intracutaneous
Nose, Throat, Teeth
Previous Ops.
Findings

TREATMENT
Elimination of
Desensitization to
Vaccine
Drugs
Removal foci
Other treatment
Duration treatment
Cooperation

RESULTS
Duration of cure
Condition
Since last seen
At present
Adrenalin
Exposure to animals and feathers
Treatment by other M. D.
Kind
Results
Surgery
Results
Change of climate
Length
Location
Results
Results in %
REMARKS:

Fig. 2.—Summarizing card made out for each patient.

Table 2 analyzes the follow-up in each group. This shows that almost all of those who were entirely symptom free in 1935 were still entirely or almost entirely relieved. One of the 2 who died was accidentally killed, and the other died of lobar pneumonia. Unfortunately, we are unable to trace 9 of these 45 patients.

Nineteen of the 104 patients previously classified as improved have by now been symptom free for over a year, but 4 are worse and 6 have died. Of the 37 patients previously reported as unimproved, only 9 are now improved and 8 have died.

The best results were obtained in youngsters and especially in those in whom the offending cause was found and eliminated.

Survey of Entire Group of 459 Cases.—In addition to the 207 patients just analyzed, an additional 252 patients have been added, this making a total of 459. The second group has been under observation for from one to eight years.

In the 1935 report, we divided our cases into "extrinsic" and "intrinsic," in accordance with the suggestion of Rackemann. An "extrinsic" patient is one who has been found hypersensitive to one or more allergens. All patients whose causative allergens were not discovered were placed in the "intrinsic" group, wherein it is thought that the asthma is due to something within the body, possibly bacteria. The best results were naturally found in the "extrinsic" group.

TABLE 1.—*Follow-Up After Seven Years of 207 Cases of Bronchial Asthma, with Results of Treatment*

	1935		1942	
Results	Number of Cases	Percentage	Number of Cases	Percentage
100% ("cured")	45	21.7	43	24.3
Improved	104	50.2	82	46.3
Unimproved	37	18.0	16	9.0
Dead	21	10.0	36	20.3
Not traced	..	....	30	....
Total	207	99.9	207	99.9

TABLE 2.—*1942 Follow-Up of Groups of Cases Reported in 1935*

		Results in 1942				
Results	1935 Number of Cases	100% ("Cured")	Improved	Unimproved	Dead	Not Traced
100% ("cured")	45	23	11 (90-95% relieved)	..	2	9
Improved	104	19	63	4	6	12
Unimproved	37	1	8	12	8	8

In the present study we have classified the patients as "paroxysmal" or "chronic," because we believe that this grouping is superior in that it can be made at the time of the first visit and because it indicates a much more accurate prognosis than any other classification. Our good results are usually obtained in the paroxysmal group. Chronic asthma is often complicated by emphysema and chronic bronchitis. While it is true that most patients with paroxysmal asthma show definite positive cutaneous reactions and are therefore classed as "extrinsic," this is not always the case, since some of these patients classified as "extrinsic" have acquired chronic asthma.

Table 3 refers to the sex and age of onset in the entire group. For some unknown reason males predominate in the paroxysmal group and females in the chronic. The most outstanding observation is the high incidence of paroxysmal asthma in the first decade, comprising 144 of the 459 cases. The number of paroxysmal cases diminishes as age increases, and cases are

uncommon in the age group past 50; on the other hand, chronic asthma occurs at all ages, even in patients whose asthma begins in the first ten years of life.

The results of treatment are found in table 4, which reveals that the number of those who obtained 100 per cent relief from symptoms was far greater in the paroxysmal group, 93 to 4; likewise, this group included 173 patients who were improved as compared to 72 in the chronic group. Death was much more common among the chronic group; 37 of 161 patients with chronic asthma died, an incidence of approximately 23 per cent as opposed to only 11 of 298 patients with paroxysmal asthma (3.7 per cent).

One also notes that the best results are obtained in those whose paroxysmal asthma begins in the first decade of life. The prospect for complete relief or improvement lessens with increasing age, although the table shows that this is not entirely true in each decade. The prognosis is especially good for paroxysmal asthma in the age group 20 to 29.

Table 5 summarizes the cause of death in the 48 cases. In 21 instances, death was known or presumed to be due to asthma. When a patient with severe asthma died and the cause of death was not stated and there were no other known contributory factors, asthma was presumed to be the cause of death. This may, of course,

TABLE 3.—*Sex and Age of Onset of 459 Cases of Bronchial Asthma (Entire Group)*

	Paroxysmal		Chronic	
Age at Onset	Male	Female	Male	Female
0- 9	95	49	13	25
10-19	16	28	12	16
20-29	18	32	5	17
30-39	17	14	9	14
40-49	10	14	15	14
50-59	3	2	7	10
60-69	..	..	2	2
Totals	159	139	63	98

not be correct, and our percentage in this group is probably too high. Sixteen patients died who had both asthma and some other serious condition, e. g. hypertension, cerebral hemorrhage, pneumonia or cardiac decompensation. The asthma of the other 11 patients had been entirely or almost entirely relieved and they might well be classified in the 100 per cent or improved group, but death occurred from some cause other than asthma, e. g. accident, pneumonia, meningitis, carcinoma or bleeding peptic ulcer.

In the first group of 21 who died during asthmatic seizures, morphine was known to have been injected in 6 shortly before death, and one may well believe that others in the group may also have received this drug. Autopsy on 2 of those who received morphine revealed almost complete blocking by mucous plugs of the smaller bronchi and bronchioles. Our own experience and that of others has led us to the conclusion that morphine should never be given during an attack of bronchial asthma. Morphine probably kills patients with asthma by depressing the cough reflex so that they cannot cough up the sticky sputum which blocks the air passages; it probably harms also by depressing the cerebral respiratory center and, in some instances, by a hypersensitivity to the drug. We might add that since we abandoned the use of morphine some ten years ago no patient under our care has died of asthma.

Table 6 summarizes the results of therapy in 459 cases. Ninety-seven of the patients obtained 100 per cent relief (21.1 per cent); 245 patients showed improvement varying from 25 to 95 per cent (53.3 per cent); 69 patients were unimproved (15.1 per cent), and 48 were dead (10.4 per cent). The excellent results obtained in the paroxysmal group are clearly shown.

TABLE 4.—*Results of Treatment in 459 Cases of Bronchial Asthma*

	Paroxysmal				Chronic			
Age at Onset	100% ("Cured")	Improved	Unimproved	Dead	100% ("Cured")	Improved	Unimproved	Dead
0- 9	55	81	5	3	..	23	9	5
10-19	9	29	6	..	2	13	9	4
20-29	17	37	4	2	..	8	10	4
30-39	8	17	5	1	..	11	7	6
40-49	4	17	..	3	2	7	9	11
50-59	..	2	1	2	..	9	4	4
60-69	..	..	..	..	..	1	..	3
Totals	93	173	21	11	4	72	48	37

REVIEW OF THE LITERATURE

The task of gathering statistics as to results of treatment in large series of cases is so great that very few reports can be found. The early studies of Walker,[4] Larsen and Bell,[5] and Rowe [6] either gave no tables of results or the duration of observation was less than one year, which we believe to be the minimum requirement. Menagh [7] in a study of 300 patients with asthma reported that 85 were well, 83 improved and 38 not improved. He states that surgery of the nose and throat cleared up 31 per cent of his cases and that vaccines aided another 44 per cent. Browning [8] in a series of 244 cases of bronchial asthma obtained 95 to 100 per cent relief in 89 instances and 75 to 95 per cent

TABLE 5.—*Causes of Death in Bronchial Asthma*

1. Asthma main or sole cause	21 cases*
2. Asthma a contributory factor	16 cases
3. Other causes (asthma not a factor)	11 cases

* Morphine known to have been injected prior to death in 6 of these patients.

TABLE 6.—*Summary of Results of Therapy in 459 Cases of Bronchial Asthma*

	100% ("Cured")	Improved	Unimproved	Dead	Total
Paroxysmal	93	173	21	11	298
Chronic	4	72	48	37	161
Total	97	245	69	48	459

in another 117. He points out that the shorter the duration the better the prognosis and therefore urges early examination. His results with patients whose

4. Walker, I. C.: Clinical Study of Four Hundred Patients with Bronchial Asthma, Boston M. & S. J. **179:** 288 (Aug. 29) 1918.

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6. Rowe, A. H.: Bronchial Asthma in Children and Young Adults, Am. J. Dis. Child. **31:** 51 (Jan.) 1926.

7. Menagh, F. R.: The Results of Treatment in Bronchial Asthma, Ann. Clin. Med. **5:** 656 (Jan.) 1927.

8. Browning, W. H.: The Treatment of Bronchial Asthma in Two Hundred and Forty-Four Cases, New Orleans M. & S. J. **90:** 269 (Nov.) 1937.

asthma begins in the first ten years of life are, like those of ours, much the best obtained in any decade.

Claude [9] states that thoracic deformity is especially common when asthma begins during infancy. While Edrington [10] gives no definite statistics, he does say that results obtained by the present day treatment are a vast improvement over those obtained twenty or thirty years ago and that the outlook for the asthmatic patient is not nearly as hopeless as it was in former years. Time and a better understanding of many factors concerned will still further improve our results. Copeland and Keating [11] obtained good results in 80 per cent of 58 children with pollen asthma and hay fever.

We are especially indebted to Rackemann for his surveys as to results of treatment. In 1927 he reported a series of 1,074 private and clinic patients with asthma who had been followed for at least two years.[12] His results were about the same as ours, i. e. about 20 per cent of his patients are in the "cured" class; another 50 per cent are more or less improved; about 20 per cent are no better, and the other 10 per cent are dead. In his series, as in ours, the percentage of "cured" and improved patients is high among those whose asthma begins in the first decade and decreases with each decade. In both series the best results occur in those cases in which the cause can be found and can be eliminated.

In 1928 [13] and in 1932 [14] Rackemann reviewed his so-called cured group and found that 49 of these 213 patients had had a relapse. From this it is apparent that Vander Veer [15] was probably correct when he stated that "once an asthmatic, a patient is usually a potential asthmatic for the rest of his life." Or, as Rackemann puts it, "the results in the extrinsic group show that cure has been accomplished by the removal of the trigger which fired the attack, but obviously the gun remains loaded in most and probably in all cases. Fundamental allergy is evidently a remarkably persistent trait."

The good results reported in this country by many observers are apparently not obtained by some in other lands. Witts [16] of London stated that after five years of work at the asthma clinic he was very much dissatisfied with the treatment of asthma. He said, "Many American books on allergy read like a detective story. One sees the allergist studying the most intimate details of the patient's life, entering his bedroom and holiday camp, placing in position his greased slides and Petri dishes, estimating the leukopenic index and supervising an elimination diet until the offending allergen is tracked down. Like psychoanalysis, it makes exciting reading, but it is difficult, if not impossible, to apply on a large scale in practice. In any event, the detection of allergens is very different from the cure of asthma." Most of us, I am glad to say, do not agree with these amusing remarks.

9. Claude, F.: The Prognosis of Asthma in Infancy, Bruxelles-méd. **18:** 1054 (June) 1938.
10. Edrington, N. K.: Bronchial Asthma, New Orleans M. & S. J. **92:** 32 (July) 1939.
11. Copeland, S. C., and Keating, J. P.: Pollen Asthma, Pennsylvania M. J. **43:** 1137 (May) 1940.
12. Rackemann, F. M.: Studies in Asthma: I. A Clinical Survey of 1,074 Patients with Asthma Followed for Two Years, J. Lab. & Clin. Med. **12:** 1185 (Sept.) 1927.
13. Rackemann, F. M.: Studies in Asthma: II. An Analysis of Two Hundred and Thirteen Cases in Which Patients Were Relieved for More Than Two Years, Arch. Int. Med. **41:** 346 (March) 1928.
14. Rackemann, F. M.: Asthma: Two Hundred and Thirteen "Cured" Patients Followed up Four Years Later, Arch. Int. Med. **50:** 819 (Dec.) 1932.
15. Vander Veer, A., Jr.: The Present Status of the Treatment of Hay Fever and Asthma, Am. J. M. Sc. **164:** 97 (July) 1922.
16. Rackemann, F. M.; Witts, L. J., and Boland, E. R.: Discussion on Certain Aspects of the Problem of Asthma, Proc. Roy. Soc. Med. **31:** 529 (Jan.) 1938.

COMMENT

Despite the probability that the tendency to asthma continues to exist in all asthmatic patients, one must not be downcast. On the contrary, we have shown that by the allergic method of treatment, if carefully supervised and if coupled with good hygienic measures, the results obtained are often phenomenal and long lasting. Not 1 of 36 patients reported as being entirely symptom free in 1935 had a relapse to any extent in the past seven years, and many of the patients previously reported to have improved are now free from asthma.

The outstanding finding in these and in similar studies has been the excellent results obtained in those whose asthma starts in early life, and especially in those whose causative factor has been removed. When we compare the paroxysmal group with the chronic, we are struck with the great difference between the two. The results in the paroxysmal group are excellent, as contrasted to the results in those in whom symptoms are more or less constant. Improvement occurs in about half of the chronic cases, but complete relief is rarely obtained.

It would seem, then, that three important observations can be made. In the first place, one should try to prevent the very onset of asthma; this is especially successful if children of allergic parents are shielded from known causes of asthma, e. g. pets and feather pillows. Second, if allergic symptoms begin, cutaneous tests and other methods of allergic survey should be carried out at once; it is sheer folly to wait until chest deformities, bronchitis and emphysema occur and the symptoms have become chronic. Lastly, since allergic persons may suffer a relapse, they should be kept under observation as long as possible. They may not need treatment but they should not be discharged. They should report for reexamination every few months at first and then perhaps once a year. Patients are very apt to become careless of their environment or diet.

SUMMARY AND CONCLUSIONS

1. A follow-up study in 207 cases of bronchial asthma revealed that after an additional seven years almost all patients who previously were symptom free were still in excellent condition. Nineteen of 104 patients previously reported as improved are now 100 per cent relieved, and a few are worse or have died. Those who were unimproved in 1935 were for the most part still unimproved or had died.

2. In addition to these 207 cases, an additional 252 patients have been added to the study, making a total of 459 patients who have been under observation from one to twenty years.

3. Because of the simplicity and because of the more accurate prognosis, the cases have been classified as "paroxysmal" and "chronic." The paroxysmal cases occur chiefly in early life, but chronic asthma is prevalent at any age.

4. Ninety-three of the 298 patients with paroxysmal asthma obtained 100 per cent relief from symptoms as compared to only 4 of the 161 patients with chronic asthma; the percentage of improvement was also much higher in the paroxysmal group, while death occurred in 23 per cent of the chronic cases as contrasted to only 3.7 per cent in the paroxysmal group.

5. The best results are obtained in those who have paroxysmal asthma caused by some allergen which can be found and which can be eliminated. Symptoms in these successful cases are apt to begin in the first decade of life.

6. Death occurred in 48 cases, or approximately 10 per cent of the entire series. Of these, asthma was the sole or main cause in 21 cases and was a contributory factor in another 16 instances. The other 11 fatalities occurred accidentally or from disease not related to asthma.

7. Morphine was known to have been given prior to death in 6 cases, and probably caused death by preventing the expulsion of obstructing mucous plugs. Since we have abandoned the use of morphine several years ago we have not had a fatality due to asthma.

8. To prevent chronic asthma, with its relatively poor prognosis, preventive measures should be instituted in the children of allergic parents, and an allergic survey should be made at once if symptoms begin.

185 North Wabash Avenue.

ABSTRACT OF DISCUSSION

DR. RALPH G. MILLS, Decatur, Ill.: There is no such thing as a normal lung unless one accepts as normal the organs of an infant at birth. Immediately after birth the lung becomes the scene of conflict between invading bacteria and the tissue protecting mechanism. The changes that result from this and similar assaults make it possible for asthma to develop in certain individuals. Asthma does not appear immediately after birth but at a somewhat later date. This may be a few months or it may be many years. Sufficient time must have elapsed for organic change to take place as well as disturbed physiology. In some way H substance, perhaps histamine, is formed during antigen-antibody contact and thus is initiated the sequence of events called asthma. The neutralization of this substance and the elimination of the product of its action—mainly mucus—is the ultimate aim of treatment. The earlier this is accomplished, the lighter the attack. I wish the authors had presented more in detail the methods employed in counteracting the effects of histamine. One might roughly classify the methods enumerated into two groups. All those are good that loosen the mucous plugs in the bronchioles, and those are useless that fail to do so. Morphine is properly placed in the latter class. I am none too sure about oxygen and helium. They relieve distress, it is true, but chiefly by reducing the tendency to cough, a mechanism by which drowning is avoided. Iodized oil introduced into the bronchi does not arouse my enthusiasm. The mention of intravenous dextrose is proper, for there is much evidence that blood sugar levels may run quite low at times. An attack of asthma is a physical ordeal, and the body needs additional calories. No mention was made of glandular therapy. I feel that thyroid should surely be mentioned, and possibly also adrenal and anterior pituitary. The results of treatment are seemingly better in the second period than in the first. Definite progress is being made in therapy, and it is to be expected that later reports will be even better.

DR. GEORGE F. HARSH, San Diego, Calif.: A study like this is especially valuable, because I find among my colleagues a most distressing pessimism about the results of treatment of allergic disorders. The authors properly warn against the use of morphine. I was trained in a school which taught that you should never use morphine in a case of asthma. I experimented gingerly and I believe I have detected a certain small group of asthmatic patients for whom the use of morphine is justifiable, and that is the type of patient who is going along perfectly normally and then suddenly gets a violent attack of asthma. He is terrified. He thinks he is going to die. Epinephrine will relieve him partially, but he is still almost literally scared to death. A small dose of morphine may completely abort that patient's attack. If it comes back as soon as the effect of the opiate has worn off, morphine should not be repeated. Some physicians use apomorphine. I should like to ask the authors whether there is not the same danger with apopmorphine as with morphine. There is one other drug that is at least as dangerous as morphine, and that is atropine. The one asthmatic patient for whom I had the misfortune of officiating at death was given atropine. This patient, incidentally, was also unable to tolerate iodides, so that adequate treatment of his asthma was seriously hampered. One method of treatment which is conspicuous by its absence in this discussion is "change of climate." That seems to be the treatment *par excellence* in the mind of the public and in the minds of many physicians. I live in a part of the country where we get a great many patients for whom this treatment has been advised. A change of climate is a drastic form of treatment. A man who is established in a community has to leave his friends and his job and dispose of his property at a loss. The very type of patient who would be a candidate for such a drastic form of treatment is the one who is likely not to benefit by it. In other words, the patient with severe asthma is the one who is apt to become sensitive to whatever there is in the environment to be sensitive to. After a change of climate he may for a short time show some improvement, but soon the old condition will return.

DR. HERBERT F. ROBB, Belleville, Mich.: I believe the older practitioner will recognize that there are more cases of asthma today than there were twenty-five years ago. In the etiology of asthma we recognize the hereditary factors along with others in the cause of allergy. We should also recognize that asthma is a psychosomatic disease and as such is under a greater influence in our urban civilization than it was back in the agricultural era. When we consider that the individual is developed from the union of two microscopic cells planted in the uterus of the mother, grown there for nine months and then cast out into a misunderstanding world, we cannot help but realize the innumerable and varied environmental forces to which the human organism is subjected. Before and after birth the individual is dominated by five forces: hunger—hunger for air, water, food and chemicals; sex, a force which becomes dominant in the parents and individual at the age of puberty; intelligence, which may be negative or positive, and social and economic forces which are positive or negative. In asthma of the child we may consider that it is possibly the functional and organic result of a psychosomatic problem in the parents. In the urban centers there is a reduced birth rate and the greater problem of birth control. It would be well in our study of the etiologic factors in the cause of asthma to consider the sex problem between husband and wife to discover any psychic conflicts or sexual maladjustments which may be factors in the development or exacerbation of this disease.

DR. LEON UNGER, Chicago: There are three schools of thought with relation to allergy and psychoneurotic disturbances. There are those who believe that the psychoneurotic effects are most important, those who pay no attention whatsoever to them, and those who believe that the psychoneurotic influences do play a part. I belong to the latter group. There is no doubt that psychic and neurotic influences increase the severity and the frequency of attacks of asthma, but I deny emphatically that psychosomatic influences can initiate asthma. In treatment we must make every effort to reduce the psychosomatic disturbances in order to reduce the frequency and severity of the attacks. The role of histamine or H substance in asthma has never been proved. We believe that, when the antigen-antibody contact is made, something similar to histamine is elaborated. It probably is some substance which is related to histamine to which the name H substance is given. Dr. Mills spoke of the method of neutralizing this substance. That is theoretical. However, his point of dividing the methods for counteracting histamine into those which loosen mucus in the bronchioles and those that do not is good, because death in asthma and the symptoms in asthma are definitely due to the obstruction in the bronchioles, and anything one can do to increase the lumen of the bronchioles is beneficial to the asthmatic. Morphine may kill the patient because it prevents the expulsion of these mucous plugs. As to the role of oxygen and helium, I too am not sure. We use it in our hospital in Chicago. Helium conveys the oxygen more readily into the bronchioles. I used iodized oil for treatment years ago but have stopped using it. Dextrose intravenously is excellent for two reasons: First of all, it is nourishing and, second, in severe cases, the addition of 1 cc. of 1:1,000 epinephrine into a liter of 5 per cent dextrose often gives good results. The use of the endocrines

has been disappointing. Solution of posterior pituitary has not given good results. We advise change of climate if a patient has been under treatment for six months or a year and has followed the treatment intelligently but still has asthma. I want to emphasize two things: Don't use morphine in bronchial asthma; use it in cardiac asthma. Second, see these patients early, before their condition becomes chronic, and good results will follow, but if one waits until they are in the chronic stage, one will have a problem on one's hands.

PULSATING EXOPHTHALMOS

REVIEW OF ALL REPORTED CASES

J. D. MARTIN JR., M.D.
AND
ROBERT F. MABON, M.D.
ATLANTA, GA.

Unilateral pulsating exophthalmos was first described by Benjamin Travers in 1809.[1] Since then there have been approximately 812 cases reported in the literature. Any retrobulbar mass may produce an exophthalmos, but usually vascular disease is the basis for the pulsating form. The bruit and pulsations of the orbit usually occur from the synchronous movements of the blood through an arteriovenous fistula. These pathologic processes have been verified by many autopsies.

An attempt is being made to present evidence justifying the diagnosis of these conditions and to report a series of cases. A complete summary of all additional reports since Locke's review is submitted.

Travers's conception of the etiology was incorrect, although it was realized that compression of the common carotid caused a cessation of the bruit and a decrease in the degree of the exophthalmos. In 1812 Dalrymple reported a second case of this nature. Before 1823 it was believed that the condition was due to a cirsoid aneurysm, but Guthrie found at autopsy an aneurysm of the ophthalmic artery. In 1835 a new theory was formulated by finding at autopsy a communication between the cavernous sinus and the internal carotid artery. Warren in 1837 described the first case which was produced by trauma. Burke in 1839 confirmed Guthrie's findings in a second autopsy. Nunneley in 1862 believed that the etiologic factor was such a fistula. In 1880 Sattler concluded from a review of the literature that the cause was due to an abnormal arteriovenous communication. De Schweinitz and Holloway in 1907 [1] reviewed and clarified the reports of these conditions. Locke [1] in 1924 made a complete review of the literature to this date and summarized the methods of treatment.[2]

ANATOMIC DISCUSSION

The majority of the cases of pulsating exophthalmos are unilateral. The most frequent causes of a nonpulsating unilateral exophthalmos are retrobulbar tumors of soft tissues, bony orbital tumors or vascular lesions such as varicocele of the ophthalmic veins. Infections of the sinuses, soft tissues and bones of the orbit may produce an exophthalmos. Prominence of the eye may occur as a result of an anterior staphyloma or a high myopia.

The pulsating form usually follows trauma and is the result of a fistula between the internal carotid artery and the cavernous sinus. In some instances a fracture through the base of the skull involving the body of the sphenoid may be demonstrated. It is in this relatively immobile area that the greatest damage to the vessels occurs. Pulsating exophthalmos may result from penetrating wounds in this region. Spontaneous cases may occur from rupture of the artery within the sinus, caused by arteriosclerotic plaques, miliary septic aneurysms or congenital weakness of the vessel wall.

The relations of the internal carotid artery and cavernous sinus are peculiar in that they constitute the only example of an artery lying within and entirely surrounded by a venous channel. This arrangement may permit the formation of arteriovenous fistulas with a minimum of trauma.

The cavernous sinus is an irregularly shaped venous space situated between the meningeal and periosteal layers of the dura mater on the side of the body of the sphenoid bone.[3] It extends from the medial end of the superior orbital fissure in front to the apex of the petrous portion of the temporal bone behind. Its lateral wall contains the oculomotor and trochlear and the ophthalmic division of the trigeminus nerves, in order from above downward. The internal carotid artery and abducens nerve are contained in the thinner medial wall of the sinus. The two cavernous sinuses communicate across the midline by the small intercavernous sinuses situated before and behind the hypophysis.

The internal carotid artery enters the floor of the base of the skull through the foramen lacerum in the temporal bone (ensheathed by a prolongation downward of the dura).

Turning forward, it traverses the cavernous sinus, separated only by a covering of endothelium. Near the anterior end of the venous space, it curves upward along the medial side of the anterior clinoid process, gives off the ophthalmic artery and perforates the dura mater again to unite with its fellow of the opposite side in the circle of Willis. The ophthalmic artery enters the orbital cavity through the optic foramen below and lateral to the optic nerve.

Anteriorly the two ophthalmic veins lie within the orbital cavity and join the sinus either separately or by a common trunk.

Posteriorly the cavernous sinus is drained through the superior and inferior petrosal sinuses, which in turn empty into the lateral sinuses.

The pathologic physiology of pulsating exophthalmos resulting from an arteriovenous fistula in the cavernous sinus is apparent. There is a difference in pressure in the two vascular channels and the venous communications of the sinus. A rupture results in a sudden engorgement of the venous space with arterial blood under high pressure. There is a retrograde flow into the ophthalmic veins, with transmitted arterial pulsations and a venous engorgement of the orbital contents and eyelids. These changes may occur to a less degree on the opposite side as a result of the aforementioned communications between the two cavernous sinuses.

Help was received from Dr. Roy Robertson in the preparation of this paper.

From the Department of Surgery of Emory University School of Medicine.

Read before the Section on Surgery, General and Abdominal, at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1942.

1. Locke, E. C., Jr.: Intracranial Arteriovenous Aneurysm of Pulsating Exophthalmos, Ann. Surg. **80**: 1-24 (July) 1924.

2. A complete bibliography of all reported cases since 1924 can be obtained from the authors.

3. Gray, Henry: Anatomy of the Human Body, ed. 22, Philadelphia, Lea & Febiger, 1930, p. 658.

After ligation of the cervical portion of the internal carotid, collateral circulation is afforded through the circle of Willis. In the ligation of the common carotid, further collateral circulation is obtained through a retrograde flow from the external carotid into the internal carotid on the same side. In many cases there is sufficient collateral to bring about incomplete regression or recurrence of symptoms.

TABLE 1.—*Symptoms in Order of Frequency as Shown in Cases in Literature Since Locke's Review*

Symptoms Reported in 224 Cases	
Symptom	Number
Bruit	191
Pulsation	179
Chemosis	159
Diplopia	76
Headache	71
Visual disturbance	66

DIAGNOSIS

The diagnosis of unilateral exophthalmos is usually easy, depending on the degree of proptosis. It has been noted in many cases that pulsation does not always exist. In those which occur spontaneously, pulsation may be absent. Following head injuries a bruit, thrill and pulsation usually are present. The symptoms most often encountered are headache, disturbance in vision and intracranial noises. The sounds may vary from minor sensations to an almost continuous roaring. The visual field may show a wide range of disturbance. Diplopia may result from an increase in internal or extraocular pressures. The presence of chemosis accounts for some of these changes. Blindness may be due to atrophy of the optic nerve, to glaucoma or to cataract.[4]

The extrinsic movements of the eye are limited by the proptosis and the alterations in the nerve mechanism of the extraocular muscles. The retinal findings are not constant and depend on the duration of symptoms. Compression of the common carotid artery will result in a cessation of a bruit, thrill and pulsation when present. Arteriograms [5] may be obtained by the injection of thorium dioxide in the carotid arteries. This procedure is useful in the diagnosis of obscure cases. The radioactivity of this or similar substances should limit its use.

TABLE 2.—*Results in Treatment of 188 Cases*
(Total Reported Since 1924)

Method Used	No. of Cases	Cured	Improved	Unimproved	Deaths	Hemiplegia
Ligation of internal carotid artery	47	25	15	3	2	2
Ligation of common carotid artery	43	30	9	1	3	..
Combination of ligations (veins and arteries)	41	27	11	0	2	1
Direct intracranial ligation (Dandy)	6	4	..	..	2	..
Nonoperative treatment	51	9	22	17	3	..

4. Dupuy-Dutemps, M. L.: Pulsating Exophthalmos with Glaucoma: Ligation of Internal Carotid, Bull. Soc. d'opht. de Paris, March 1927, pp. 136-143.

5. Terry, T. L., and Mysel, Philip: Pulsating Exophthalmos Due to Internal Carotid-Jugular Aneurysm: Use of Thorium Dioxide Solution in Localization, J. A. M. A. **103**: 1036-1041 (Oct. 6) 1934.

REPORT OF CASES

CASE 1.—E. C., a Negro aged 62, admitted to Emory University Division of Grady Hospital, Dec. 26, 1940, was struck by an automobile in October 1940 and was temporarily unconscious. He was seen immediately in the outpatient clinic and at that time had regained consciousness. A small scalp wound was then sutured. There were no complaints until November, when he heard a loud noise in his left ear which was synchronous with the heart beat. Soon afterward his left eyelid gradually increased in size until he was unable to close it. There were no visual defects. A definite chemosis of the left eye was noted with a protrusion of the orbital contents, which did not pulsate. Extraocular movements were well performed. Both pupils were round, regular in size and reacted to light. There was a moderate thrill and bruit heard over the left supraorbital ridge. Roentgenograms of the skull revealed a long, linear fracture arising in the region of the left frontoparietal bone near the junction of the sphenoid. Blood pressure on admission was 150 systolic and 70 diastolic. Daily digital compressions of the left carotid artery were begun. Following this there was a slight decrease in the swelling and chemosis of the eye.

A partial occlusion of the left common carotid artery was made with an aluminum band. On Jan. 21, 1941 the left common carotid artery was ligated with braided silk, proximal to the site of the previously applied band. No evidence of cerebral anemia was manifested following this procedure. The bruit was inaudible and the chemosis almost subsided. Two months later no return of symptoms had been noted.

Fig. 1 (case 1).—Exophthalmos with pronounced chemosis before operation.

CASE 2.—F. S., a Negro aged 24, admitted to Emory University Division of Grady Hospital, July 26, 1936, was struck over the right eye when he was overturned in a truck on May 2, 1936. He received a small abrasion over the eye but did not lose consciousness. A swelling was present on the upper eyelid which continued to increase in size. About a month before he was admitted to the hospital the lower lid became swollen and edematous. The patient complained of a continuous noise within the cranium. Physical examination was negative except for the right eye. There was definite proptosis with a protrusion of the lower bulbar conjunctiva. Movements of the eye were somewhat slow; the pupils were round and active, but the right was slightly larger and more sluggish. Tension in the right eye was 25 mm. and in the left eye 20 mm. In the right fundus was a large flamelike hemorrhage on the upper and inner disk margin. The veins and artery ratio was 4 to 1 but no pulsations were noted. There was sclerosis in the retinal vessels, more pronounced in the superior nasal artery. The left fundus was essentially negative except for a slight sclerosis. The vein and artery ratio in the left eye was 3 to 2. Vision was good in both eyes with no disturbances in the visual fields. A loud bruit was audible over the right eye, which disappeared on compression

of the right common carotid artery. The blood pressure in the right arm was 150 systolic and 102 diastolic. In the left arm it was 120 systolic and 80 diastolic. X-ray examination of the skull revealed a linear fracture passing from the region of the upper portion of the right supraorbital ridge obliquely upward and through the lower anterior portion of the right

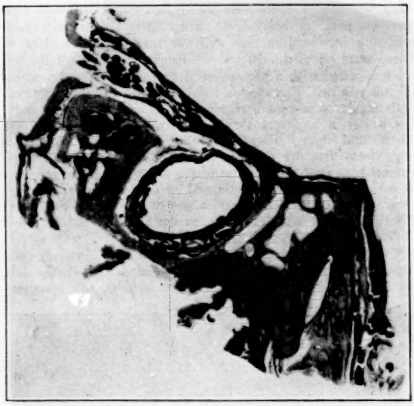

Fig. 2.—Anatomic section demonstrating internal carotid artery in the center of the cavernous sinus; also showing relative position of nerves in sinus wall.

frontal bone. There was no comminution or depression of these fragments. An area of increased density was visible in the region of the right orbit and optic foramen.

The contours of the superior orbital fissures were obliterated. Periodic digital compressions were instituted to increase collateral circulation within the brain. On August 4 the right internal carotid was ligated with two heavy braided silk ligatures. The bruit immediately stopped. Convalescence from this procedure was uneventful.

CASE 3.—J. T. B., a white man aged 43, admitted to Emory University Hospital on Nov. 3, 1938, stated that the

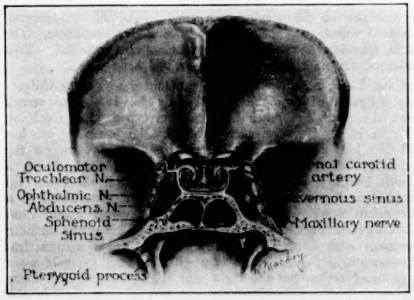

Fig. 3.—Relationship of the sinus to the arteries and nerves and the reflections of the dura.

left eye suddenly became swollen eight months prior to admission and began to protrude from its normal position. Shortly after this a roaring was noted which could be controlled by pressure on the left side of the neck. The patient complained of severe headaches and had been treated for hypertension several months before the onset of the exophthalmos. There was no history of trauma. Physical examination was essentially negative except for hypertension. The blood pressure in the left arm was 170 systolic and 114 diastolic. In the right arm the blood pressure was 180 systolic and 110 diastolic. The left eye protruded definitely. There was a chemosis and engorgement of the conjunctival vessels. Compression was applied for five minute intervals on the left common carotid three times daily for about a week. On November 8 he was operated on by Dr. D. C. Elkin. The left common carotid artery was completely occluded by an aluminum band. Postoperative convalescence was satisfactory. The exophthalmos improved considerably but the venous congestion in the conjunctiva still remained. At the present time no change in his condition has been noted.

CASE 4.—E. M., a white man aged 22, admitted to Emory University Hospital on March 7, 1936, had been in an automobile accident six months before. Following this a roaring noise was heard in the right ear. There was a swelling of both eyes, more pronounced in the right. The exact nature of the injury was not determined at the time of the accident, and the patient did not interrupt his usual activities.

The patient was well developed and well nourished and appeared normal in every respect except for the eyes. There was some edema of both eyes, the right being more prominent

Fig. 4 (case 5).—Tortuosity of vessels occupying the orbital fossa.

with edema of both upper and lower lids. The ciliary vessels of the right eye were engorged. Vision was not affected. The fundi were normal except for venous engorgement. Pulsations of the eye were not present. A thrill was felt and a bruit was heard over the entire skull, most pronounced over the supraorbital region on the right side. The blood pressure was normal. It was thought that the patient probably had a traumatic arteriovenous fistula involving the cavernous sinus.

Preliminary preparations were made for ligation of the carotid artery by compression of the vessels in the neck to stimulate collateral circulation in the brain. After about ten days, on April 27, ligation of the right internal carotid artery was done. A small Matas aluminum band was placed around the internal carotid artery, which completely compressed it at the bifurcation of the common carotid artery. There was an immediate cessation of the thrill and bruit in the region of the right eye. No untoward symptoms were noted. For some time the patient noticed that on severe exertion a numbness occurred in the left side of the body, which disappeared on resting. No motor symptoms were ever exhibited. His condition in July 1941 was still unchanged.

CASE 5.—J. D., a white man aged 33, admitted to Emory University Hospital on July 8, 1940, was shot in the left eye thirteen years before and removal of the eye was necessary. Six years before admission he noticed a mass beneath the eyelid which had gradually increased in size. On examination there was a mass which filled the entire orbital fossa and protruded from beneath the lid about 3 cm. There was a definite dilata-

tion of the superficial vessels both on the surface of this mass and also to the outer side of the orbital fossa. There was a palpable thrill and bruit heard over this area. This was stopped by pressure over the common carotid artery. The remainder of the physical examination was negative. On July 12 a partial occlusion of the left common carotid artery was made with a metal band by Dr. D. C. Elkin. Three days later the artery was completely occluded with heavy braided silk. On July 15 the entire mass of veins and arteries were removed through an incision beneath the lid. There were multiple communications between the ophthalmic arteries and veins. Convalescence was uneventful except for some purulent drainage, which had cleared up on Aug. 1, 1940, when he was dismissed from the hospital.

This case presents an example of traumatic unilateral exophthalmos with symptoms usually seen in ones involving the deeper structures. The previous removal of the eye permitted a more accessible approach to the arteriovenous fistula and allowed for the usual treatment for such conditions.

TREATMENT

The treatment of arteriovenous aneurysm of the cavernous sinus and the branches of the internal carotid artery cannot necessarily be approached in the manner for similar lesions elsewhere. The usual treatment for arteriovenous aneurysms is quadruple ligation with excision of the aneurysmal sac. It is obvious that the anatomic location prohibits any such procedure. Many approaches have been made to this problem, none of which are based on good reasoning. Proximal arterial

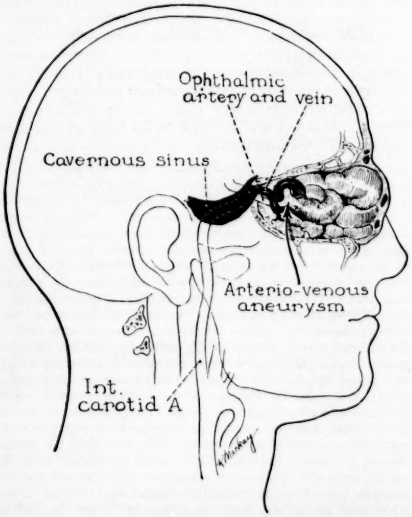

Fig. 5 (case 5).—Position of arteriovenous fistula.

ligations have been done in the majority of instances and with the greatest benefit. The common carotid artery has been ligated, as well as the internal and external, individually and concurrently. Carotid ligations have also been carried out on the contralateral side. These have been performed singly as well as simultaneously, depending on the results obtained.

Various methods of occluding the vessels have been attempted, extending from digital compression to external occlusions of the common and internal carotid with an apparatus similar to the type described by Matas.[6] Partial closures have also been made with aluminum bands, fascial grafts and other types of surgical liga-

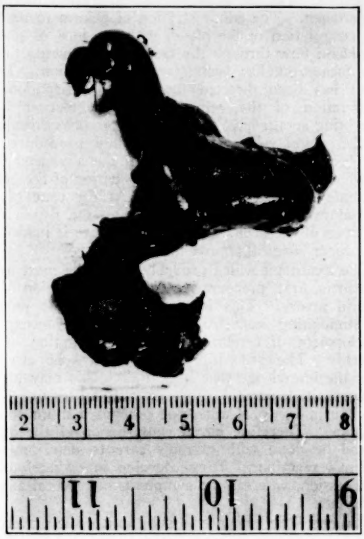

Fig. 6 (case 5).—Arteries and veins after removal.

tures such as tape and silk and, more recently, the use of cellophane.[7] The latter is used for partial occlusion. This is based on the belief that when cellophane is used it is followed by a gradual constriction. It is hoped that partial constriction may become complete after a short time. This gradual closure may lessen the likelihood of the production of cerebral anemia. Dandy [8] has devised as nearly a surgical approach to this condition as is done in ordinary arteriovenous aneurysms. His procedure is to occlude the artery as it emerges to form the circle of Willis with metal clips to obliterate the blood supply at the fistula. A previous study of the anatomy, however, has shown that the blood supply is derived, both proximally and distally to the arteriovenous communication, from one side, as well as from the face, through the communicating veins. It is also derived through the communications of the arterial supply from the circle of Willis on the opposite side. Therefore, unless a complete extirpation of the aneurysm is made along with total ligations, a cure should not be effected. Dandy reports satisfactory results using such a procedure.

6. Matas, Rudolph: Discussion on Vascular Surgery with Special Reference to the Surgery of the Carotid Tracts: The Use of Special Compressors and Aluminum Bands, Am. J. Surg. **24**: 692-698 (Dec.) 1933.

7. Pearse, H. E.: Experimental Studies on the Gradual Occlusion of Large Arteries, Ann. Surg. **112**: 923-937 (Nov.) 1940.

8. Dandy, W. E.: Carotid-Cavernous Aneurysms (Pulsating Exophthalmos), Zentralbl. f. Neurochir. **2**: 77 (March) 1937. Dandy, W. E., and Follis, R. H.: On the Pathology of Carotid-Cavernous Aneurysms (Pulsating Exophthalmos), Am. J. Ophth. **24**: 365-385 (April) 1941.

Arterial plugging[9] has been attempted by the injection of paraffin into the carotid artery with the hope that it would obliterate the arteriovenous fistula. Muscle plugs[10] have also been inserted into the artery for the same reason. These procedures for the most part have been discarded because they have not proved beneficial. Various forms of medical therapy have been undertaken. The administration of gelatin to increase the coagulation of the blood, with the idea of slowing the blood flow through the fistula and allowing thrombus formation, has been given consideration. Treatment has been directed toward the extirpation and obliteration of the veins.[11] Electrocoagulation[12] and sclerosing agents have been used to promote thrombosis of the orbital veins. The use of these procedures has not been universally adopted. In the advanced cases in which the eye has been lost, evacuation of the orbital contents has been carried out. At the time of this procedure an attack can be made on the fistula from the apex of the orbit. The exposure here is inadequate for proper surgical approach.

The treatment which probably offers the most to the patient is, first, preoperative digital compression of the carotid artery. This is undertaken for the purpose of stimulating collateral circulation, preventing the development of cerebral anemia after ligation of the carotids. The procedure should always be attended with the knowledge that some individuals may have a hypersensitive carotid sinus reflex.[13] Pressure could result in a syncopal attack or perhaps a more serious outcome. Therefore initial compression of the artery should be done with extreme care to determine the patient's reactions. These develop immediately after compression, whereas the symptoms of cerebral anemia occur late.

There is little evidence to substantiate the preference of ligation of the internal or common carotids. The latter is more commonly ligated, probably because it is more accessible. A reflux flow from the contralateral vessels through the external carotid may result in a failure of cure. If partial ligation is done it may be necessary to occlude the vessel totally after the danger of cerebral anemia is over. When an aneurysm has been present for a long time, sufficient collateral circulation will usually be established from the opposite side through the circle of Willis. Cases not benefited by ligation may be improved by a direct approach advocated by Dandy. In view of the number of cases improved and cured by proximal ligations alone, this preliminary procedure should be carried out in all instances. The results offer little support for medical therapy in the progress and termination of these conditions.

SUMMARY OF REPORTED CASES

There have been one hundred and sixty-three articles in major journals on pulsating exophthalmos since Locke's review in 1924; 224 additional cases have been reported through December 1941. Essentially all reports deal with the same problem previously discussed by Locke and others. It is noted that the choice of treatment is primarily operative. Ligation of the internal carotid was performed in 47 cases; of this number 25 were reported as cured. The common carotid was ligated in 43 instances with cures in 30. The ligation of multiple vessels, a combination of either the internal, external or common carotid and orbital veins, was carried out in 41 cases with twenty-seven cures. It is evident from such a summary that the results in all types of treatment are the same. The greatest contribution since 1924 has been, perhaps, the work of Dandy in ligating intracranially the carotid artery for the purpose of trapping the aneurysm. This procedure has been carried out six times, with 4 cases being reported as cured. It is advisable in many instances to undertake this operation when other methods fail.

CONCLUSION

In this report a complete review of the literature since 1924 has been made. This brings the total reported cases to 812. Five additional operative cases are submitted by us. An explanation for the development of these conditions is made on the basis of anatomic studies of the cavernous sinus. This is the only example of a major artery within and a part of a large venous channel. Any trauma or disease to the artery would therefore allow an interchange of arterial and venous blood between these structures; thus an arteriovenous fistula would be formed. Basal fractures involving this area should be attended with the thought that a fistula may occur. In view of the progress of the disease, early treatment, namely ligation of the carotid artery, should be undertaken before extensive proptosis develops. This would decrease the danger of further destruction and blindness. Surgical treatment is beneficial, although many cases are followed by slight improvement and sometimes no change. There is no satisfactory direct operation to obliterate the fistula. This primarily is due to its location and association with vital structures.

ABSTRACT OF DISCUSSION

DR. HARRY H. KERR, Washington, D. C.: Pulsating exophthalmos is a symptom most commonly seen in fractures of the base of the skull passing through the anterior fossa. Ligation of the common carotid artery is the best treatment. I thought we could demonstrate a direct connection between the external and internal carotid arteries intracranially. Moss and King of the Wilmer Ophthalmological Institute at Baltimore have recently shown that there is a very free communication between the external carotid artery and the ophthalmic artery. My first patient was a righthanded man aged 42 with pulsating exophthalmos of the left side. Digital compression of the common carotid demonstrated that complete occlusion promptly led to difficulty with speech and with the use of the right hand. Partial compression, however, reduced the bruit and the pulsation without producing cerebral symptoms. We therefore hit on the idea of fractional ligation. Under local anesthesia, with the patient conscious and able to cooperate, we exposed the left common carotid artery, placed a fascial band around it and constricted the artery down to a position where he had no cerebral symptoms and no disturbance of speech or function of the right hand. We then fastened the band in situ. We found that we had occluded the artery about 50 per cent. The wound was closed, and two weeks later, after experimenting with compression again, we ligated completely the common carotid artery. I reexamined this man nineteen years later and made a complete ophthalmologic study. He had remained completely cured, and his eyes were perfectly normal for a man then aged 61. I have since operated on 7 additional patients with similar results and have found that the late return of a slight bruit best heard in the neck was due to recanalization of the common

9. Dawbarn, R. H. M.: The Starvation Operation for Malignancy in the External Carotid Area, J. A. M. A. **43**: 792-795 (Sept. 17) 1904.
10. Gurdjian, E. S.: Packing of Internal Carotid Artery with Muscle in Treatment of Carotid-Cavernous Arteriovenous Aneurysm, Arch. Ophth. **19**: 936-940 (June) 1938.
11. Valiere-Vialeix: Cure of Traumatic Pulsating Exophthalmos by Ligation of Orbital Veins at Point of Entry into Orbit, Ann. d'ocul. **170**: 747-760 (Sept.) 1933.
12. Fioletov, S. S.: Treatment of Pulsating Exophthalmos by Diathermic Cautery, Sovet. vestnik oftal. **3**: 395-396, 1933.
13. Weiss, Soma; Capps, R. B.; Ferris, E. B., and Monro, Donald: Syncope and Convulsion Due to a Hyperactive Carotid Sinus Reflex, Arch. Int. Med. **58**: 407-417 (Sept.) 1936.

carotid artery, so that now, in the last few cases, in addition to fractional ligation I divide the artery. Six of the 8 cases were the result of fractured skull. One was a spontaneous pulsating exophthalmos in a woman of 73 and 1 case was due to gunshot wound from birdshot in which the other eye had been destroyed. Secondarily, ligation or division was carried out on an average of sixteen days after the first partial ligation.

DR. ALTON OCHSNER, New Orleans: There are two points that I should like to emphasize. Occasionally one will find persons whom ligation of either the internal carotid or the common carotid will not help. In such instances it is necessary to combine ligation of the carotid with the intracranial clip, as suggested by Dandy. Recently Dr. DeBakey has shown that the gradual occlusion of the artery by cellophane does not work. In an extensive experimentation he was unable to verify Pierce's work concerning this. He has had 2 patients on whom, in an attempt to increase the intracranial vascularity, he has done a sympathectomy. One of these persons was greatly improved following the sympathectomy. This is based on the observations of Gage that in patients with peripheral arteriovenous aneurysms, by decreasing the peripheral resistance and by increasing the vascularity, the aneurysm can be attacked with impunity. One of these patients was definitely improved following the sympathectomy, so that the ligation could be done safely. The other patient was cured by sympathectomy, simply indicating that by slowing the blood stream through the arteriovenous anastomosis, clotting was made possible, so that I think in the older person in whom hemiplegia is likely to occur, the use of cervicodorsal sympathectomy is of value and should be tried.

DR. JAMES RUDOLPH JAEGER, Denver: It is obvious if we remember the anatomy concerned in the carotid-cavernous arteriovenous communications that a good many of these cases will not be cured by ligating the carotid in the neck or intracranially because the internal carotid has branches inside and near the cavernous sinus which connect up with the external carotid branches, and these branches enlarge to a tremendous extent in an attempt to feed this communication. Recently I had a case which had been treated conservatively without benefit, and there is no reason why these cases should not be treated first by the conservative ligations as mentioned by the speaker. This little 11 year old fellow had had the common carotid ligated in the neck. After three months I ligated the carotid proximal to the ophthalmic artery intracranially, and there remained a tremendous bruit and a pronounced exophthalmos. At a third operation I opened the internal carotid artery in the neck and placed a muscle strip with a silver clip on the end of it, as an embolus, and then ligated the external carotid. It progressed upward to the fistula, and x-ray examinations showed the silver clip in the cavernous sinus. Before the external carotid was ligated, and before I had inserted the muscle embolus inside the internal carotid, after closing it temporarily with a tape, we could still hear the bruit, showing that the communication was being fed by the tremendously overdilated branches of the internal carotid through which the circulation had been reversed by their connections with the meningeal vessels, which are external carotid branches. This boy has stayed entirely well now for six months. His eyesight is normal. There is not the least pulsation, bruit or exophthalmos. Of course, I do not think we should completely evaluate these cases until we have observed them for five years, because frequently the circulation will be cut down through these communications to such an extent that one may think one has effected a cure; but give them time, time for the collateral circulation to develop, and a great many of them will recur.

The Indispensable Amino Acids.—If all ten of these are provided in suitable amounts, the body can form from them the remaining amino acids which enter into the composition of its proteins. The amino acids now called "indispensable," or "nutritionally essential" in the sense that they must be furnished through the nutriment, are arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine.— Sherman, Henry C.: Chemistry of Food and Nutrition, New York, Macmillan Company, 1941.

DELAY IN THE TREATMENT OF CANCER

CHARLES R. HARMS, M.D.
JULES A. PLAUT, M.D.
AND
ASHLEY W. OUGHTERSON, M.D.
NEW HAVEN, CONN.

Cancer ranks second only to cardiorenal disease in our mortality statistics. The attempt to reduce this appalling figure has been directed along two chief lines, namely the prevention and the cure of the disease. In order to accomplish either of these ends it is now generally recognized that both the medical profession and the public must be better informed regarding the cancer problem. Various national, state and local organizations have instituted educational programs better to accomplish this purpose. The need for such an educational program has been clearly recognized by many physicians for well over a century. While considerable progress has been made, we are nevertheless far short of the goal and the cancer death rate during the past century has been steadily increasing. The present study was undertaken in order better to evaluate the effectiveness of our present educational program.

It is generally recognized that the treatment of cancer by the methods which are now available must be early and adequate in order to be successful. The successful treatment of cancer may be divided into four steps, namely:

1. Early recognition of the signs and symptoms by the patient. He must at least be aware of the possibility of cancer in order that he may call on his physician for advice.

2. Early diagnosis by the physician, who must also be aware of the possibility and the steps that are necessary in order to make the diagnosis.

3. Prompt treatment, which requires the cooperation of both the patient and the physician.

4. Adequate treatment, which also requires the cooperation of the patient and specialized knowledge and technic by the doctor.

The present study is an attempt to determine the factors responsible for delay in the recognition, diagnosis and treatment of cancer. These factors cannot be adequately determined from a study of the usual clinical record; hence 158 successive cancer patients were interviewed as they were admitted to the New Haven Hospital or Tumor Clinic. Of these patients 153 were of either ward or dispensary status.

The definition of delay due either to the patient or to the physician must necessarily be arbitrary. It is also well known that the time required to recognize and diagnose a cancer which is visible on the exterior will be quite different from that on the interior of the body. However, it is not necessary to justify any arbitrary time chosen to define delay, since the facts may be so presented as to enable any one to draw his own conclusions. Furthermore, it is not our purpose

Dr. Plaut is National Cancer Council Fellow.
From the Tumor Registry of the Department of Surgery, Yale University School of Medicine.
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in this paper to make excuses for delay but rather to attempt to determine the steps which are needed in order to recognize, diagnose and treat cancer at a time when the disease is still localized and offers an opportunity for cure.

Delay by the patient may be defined for purposes of discussion as having persistent symptoms for one month or longer before consulting a physician. Delay by the physician may also be arbitrarily defined as waiting for any period longer than three weeks after the patient is first seen during which a diagnosis may be established or a consultation requested.

TABLE 1.—*Distribution of Responsibility for Delay*

Type of Cancer	Total Number of Cases	Number in Which Patient Was Responsible	Number in Which Physician Responsible	Both Patient and Physician Responsible	Median Total Delay in Months
Total number	158	85	27	43	8.46
Percentage	100%	54.8%*	17.4%*	27.8%*	
Lung	8	1	2	5	9.00
Stomach	11	3	2	5	14.00
Larynx	6	5	1	0	5.70
Esophagus	4	3	0	1	
Face and skin	17	12	0	5	12.25
Mouth, tongue, palate, alveolar ridge, hypopharynx	13	8	1	4	4.75
Lip	4	4	0	0	
Bladder	5	2	3	0	
Prostate	6	3	0	3	
Uterus	15	7	2	5	5.50
Rectum	23	11	3	8	12.00
Large bowel	13	5	5	3	12.73
Breast	23	18	3	2	12.00
Reticuloendothelial	8	3	3	2	7.00
Metastatic	1	0	1	0	
Bone	1	0	1	0	
No delay	3				

* These percentages are based on a total of 155 cases.

The distribution of the cancer by site may be seen in table 1. Three patients came immediately to the hospital for emergency treatment, 1 because of intestinal obstruction and 2 because of hemorrhage. The other 155 patients presented delay factors with responsibility distributed as follows: Eighty-five patients alone, or 54.8 per cent, were responsible for the delay, while 27 physicians, or 17.4 per cent, were responsible. Both the patient and the physician were responsible for the delay in 43 instances, or 27.8 per cent.

The patient was found to be either wholly or in part responsible for the delay in 128 instances, or 82.6 per cent. All but 7 of the 128 patient delays (121, or 94.5 per cent) were initial delays. The other 7 did not follow the physician's advice in spite of his efforts. The problem, therefore, appears to be mainly the initial delay or the interval between the onset of symptoms and the first visit to the doctor.

The cause for the delay by the patient is shown in table 2. The patients who thought their symptoms were "not serious enough" were capable of recognizing them but used poor judgment. Their information as to the possible serious nature of their symptoms was not enough to result in positive action. Those who were negligent knew the importance of their symptoms but allowed themselves to be sidetracked by other matters. The distinction between the negligent and the ignorant group is difficult to determine. Those patients were called "ignorant" who seemed to have a defect in fact as well as in judgment and who displayed that defect generally and not limited to the problems of health.

Failure to attach sufficient importance to recognized signs and symptoms accounts for most of the delay. This is primarily an educational problem which is obviously not being met by present methods. The second most important factor defined as negligence may also in large part be corrected by proper education. The economic factor accounts for 10 per cent of the group. These patients recognized their symptoms for what they were, or at least as deserving medical care, but put off seeking attention because they did not know how to pay for it. It is noteworthy that fear of cancer plays a minor role.

The effectiveness of an educational program can best be judged by the content of knowledge possessed by the group as well as its effectiveness in producing appropriate action. The following general questions were asked in order to evaluate the information regarding cancer possessed by the group: How many patients with malignant tumors think of cancer as the cause of their complaints? Only 21, or 13 per cent, answered in the affirmative. Breast cancer was responsible for 13 of these. The median delay for patients who thought they had breast cancer was 3.25 months, while the median delay for all breast cancer was 6.5 months. This suggests that the delay could be halved if all patients were aware of the significance of their symptoms. It was also found that only 42, or 26 per cent, of the patients had read about cancer. Forty of the 42 readers had obtained their information from newspapers and popular magazines, while only 2 admitted reading public health pamphlets. Only 2, or 1.2 per cent, had ever heard a lecture on cancer, and both of these had been while attending National Hospital Day. Although the entire group seemed poorly informed regarding cancer, 80 per cent thought that cancer was curable and 91 per cent thought that treatment was urgent.

Patients may be expected to delay a short time after the onset of symptoms before consulting a physician. However, the median delay for the total group was 3.77 months. They were not aware of the serious nature of their symptoms for part of this time. However, this group was aware of the seriousness of their symptoms for an average of 4.4 weeks before they consulted their physicians. Twenty-one per cent decided for themselves to consult their doctor, while the remainder were advised by their family (64 per cent) or friends (15 per cent).

TABLE 2.—*Cause for Delay*

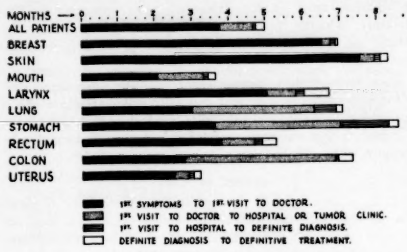
Cause for Delay	Number of Patients	Per Cent
Total	158	100
Symptoms "not serious enough"	90	56.9
Negligence	18	11.3
No delay on the part of the patient	18	11.3
Expense	16	10.1
Ignorance *	11	6.9
Fear of cancer	2	1.4
Fear of doctors	2	1.4
Christian science or other cult	1	0.6

* Limited to patients thought to be "ignorant" by observer.

Delay by the physician in making a diagnosis is also an important factor. It is appreciated that some of

this delay is unavoidable; however, every effort should be made to reduce this to a minimum. Table 1 shows that the physician alone was responsible for the delay in 27 instances (17.4 per cent) and that both the patient and the physician were responsible for delay in another 43 instances (27.8 per cent). The physician was therefore either totally or in part responsible for the delay in 45.2 per cent.

The information on which these data are based was obtained chiefly from the patient, and it is likely that



Median delay time intervals.

many of these patients did not cooperate by returning to their physicians for further study. For accurate information it would be necessary to interview both the patient and the physicain.

The median time interval from the first visit to a physician until a definite diagnosis was made was four weeks. Thus, approximately one half of the patients had a definite diagnosis within a one month interval. When these patients were grouped according to location of tumor it was found that the tumors diagnosed within one month included larynx, skin, lip, prostate, uterus and breast. Those having a delay of more than one month included lung, stomach, esophagus, mouth, colon, rectum and bladder. The longest median delay was found in lung (15.45 weeks), stomach (18.75 weeks), bladder (13.74 weeks) and colon (16.35 weeks). While a portion of this delay was inherent in the greater difficulty of making a diagnosis, it was also obvious that the greater part was due to failure to carry out the more difficult and expensive diagnostic procedures until a diagnosis was fairly certain. General physical examinations were done by 62.6 per cent of the physicians, while local examinations directed at the complaint were done in 35.5 per cent. Three patients (1.9 per cent) received no examination. A history of some kind was taken on all patients, although it was impossible to determine the quality of the history. The delay by the physician usually was due to poor advice or incorrect diagnosis as a result of failure to carry out the indicated diagnostic procedures. The most common errors were failure to take a roentgenogram or do an endoscopic examination. The median overall delay between the onset of symptoms and proper treatment for all cases was 8.46 months.

COMMENT

It is generally acknowledged that the successful treatment of cancer by the methods now available is dependent on early diagnosis and treatment. How much may be accomplished by these methods in lowering the present high mortality is unknown. Undoubtedly some cancers are so insidious in their onset that an early diagnosis and successful treatment are impossible. However, only the future can answer this question since so few patients receive treatment (8 per cent within two months) during the early stage of the disease as measured by symptoms. The medical profession has been discussing the need of public and professional education on the cancer problem for more than a century, and only recently has an attempt been made to put this into effect. The effectiveness of such an educational program can be measured only in terms of results.

The present study, which is based on 158 patients, is inadequate to give an accurate picture for the state. However, it does yield information as to the need of cancer education in the city of New Haven and particularly in the ward and dispensary groups.

Only 3 patients presented themselves for treatment within one month of the onset of symptoms, and these because of acute conditions rather than the presence of cancer. Ninety-two per cent of all patients required two months or longer and 84 per cent required three months or longer before adequate treatment was instituted. The median interval between the onset of symptoms and proper treatment was 8.46 months. These findings clearly indicate that there is unnecessary delay in obtaining proper treatment for cancer. Considering our knowledge of the growth and spread of cancer, good results in the total group cannot be expected under these circumstances.

The patient was responsible for the delay in more than three fourths of the instances. The patient was also reseponsible for the greater part of the time lost with a total median delay of 3.77 months. The physician was responsible for the delay in less than 25 per cent of the instances. The median time required by the physician to make a diagnosis was four weeks. Thus 50 per cent of all patients required more than four weeks to establish a diagnosis after first consulting their physician. It is apparent that the patient delay constitutes the major problem in the diagnosis and treatment of cancer. However, the physician also must assume a share of the responsibility.

The major cause for the patient delay is primarily lack of proper information on the cancer problem. A failure to recognize the serious nature of symptoms was responsible for 56.9 per cent of the patient delay, while expense, negligence and ignorance accounted for 10.1, 11.3 and 6.9 per cent respectively. Thus the failure of the educational program to furnish the patient with sufficient information may be held responsible for delay in at least 85 per cent of the cases.

Cancer education of this group of patients appears to be quite inadequate. Their information was obtained chiefly from newspapers; only 26 per cent had ever read about cancer, while only 1.2 per cent had ever seen a cancer pamphlet. Only 1.2 per cent had ever heard a lecture on cancer. It is apparent that more widespread and effective educational methods are needed if the public is to be made aware of cancer problems.

Delay on the part of the physician was found chiefly in cancer of the internal organs. The major part of this delay was due to the failure to request x-ray or endoscopic examination. The responsibility of the

physician cannot be fairly estimated in this study, since in most instances the physician was not interviewed and the information was obtained from the patient. The early investigation of cancer of the internal organs is a difficult problem because of the expense involved. Many of the early symptoms of cancer of the internal organs are difficult to distinguish from functional disorders, which constitute such a large proportion of the general practice of medicine. In order to evaluate this problem properly, studies should be carried on with the cooperation of physicians engaged in the general practice of medicine. This is also a problem which will grow in importance as patients present themselves for earlier diagnosis.

SUMMARY

1. Delay in the diagnosis and treatment of cancer is one of the most important factors in the failure to obtain better results by the methods of treatment now available.

2. The patient is responsible for the major part of this delay both in numbers and in the time consumed.

3. This delay by the patient is chiefly due to lack of information as to early signs and symptoms of cancer.

4. The education of the people on the cancer problem is a mutual responsibility of the public and the medical profession. This educational program is still inadequate and ineffective.

Clinical Notes, Suggestions and New Instruments

STREPTOCOCCIC MENINGITIS FOLLOWING CRANIO-CEREBRAL TRAUMA

RECOVERY FOLLOWING THE USE OF SULFAPYRIDINE AND SULFADIAZINE

JOSEPH G. RILEY, M.D., AND RICHEY L. WAUGH, M.D.
BOSTON

The introduction of the sulfonamide drugs in 1935 by Domagk[1] has radically influenced the treatment of the bacterial meningitides. Symptomatic supportive treatment and an attitude of hopeful, purposeless expectancy have given way to positive specific therapy. The efficacy of the sulfonamides can be gaged by a review of the mortality statistics of the various types of meningitides, the lowered mortality rate and the increased incidence of survival of patients reflecting clearly the worth of chemotherapy.

The mortality of epidemic cerebrospinal meningitis in the period from 1926 to 1938 was estimated at 47 per cent.[2] In 1941 it was reported as 12 per cent in a large series of unselected sulfonamide treated patients.[3] Similar reductions have taken place in the mortality rates of the other bacterial meningitides, notably of the streptococcic type.

Streptococcic meningitis prior to 1935 claimed a mortality of 95 to 97 per cent[4] despite heroic regimens of symptomatic treatment. However, in 1936, when Caussé, Loiseau and Gisselbrecht[5] reported the first case of streptococcic meningitis with recovery following the use of azosulfamide, a new therapeutic era was inaugurated. Subsequently the literature began to see many reports of cases of streptococcic meningitis in which recovery occurred following the use of specific chemotherapy.[6]

A review of these published survivals following successful positive therapy with the sulfonamides reveals that the great majority have been secondary to otitis. There has been a scarcity of published reports of cases of post-traumatic streptococcic meningitis successfully treated with the sulfonamides. In addition, most of the recovered cases appearing in the literature, whether secondary to otitis or post-traumatic in nature, are those in which sulfanilamide or azosulfamide has been used.[7]

Since later clinical investigation[8] indicates that the newer sulfonamides sulfapyridine and especially sulfadiazine are effective against streptococcic meningitis, we believe that this report of a case of post-traumatic streptococcic meningitis treated successfully with sulfadiazine is of interest:

REPORT OF CASE

W. L., a man aged 33, an iron worker, entered the hospital Feb. 2, 1942 after he had fallen from a staging, landing on his face and outstretched hands. He had been unconscious for about ten minutes.

On admission he was conscious and rational. There were multiple abrasions and areas of ecchymosis on the right side of his face and forehead. There was no bleeding from the ears but the nares showed some crusted blood. Both wrists were swollen and painful, with typical dinner fork deformities. The right elbow was swollen and painful with decided limitation of motion. The temperature was 37 C. (98.6 F.), the pulse rate 88 and the respiratory rate 22. The blood pressure was 120 systolic and 80 diastolic. Roentgenograms showed bilateral Colles' fractures, a simple fracture of the head of the right radius and a linear fracture involving the left frontal bone and extending laterally from the left frontal sinus.

Since there was no evidence of shock, both Colles' fractures were promptly reduced under intravenous pentothal sodium anesthesia.

The course for forty-eight hours after admission was uneventful. Soon thereafter, however, the patient became increasingly restless, irritable and drowsy. There was extreme rigidity of the neck and positive Kernig signs. His temperature rose to 41.2 C. (106.2 F.), with a pulse rate of 68. His respirations were deep and stertorous. The blood pressure was 200 systolic and 100 diastolic. A lumbar puncture at this time showed a spinal fluid pressure of 550 mm., with turbid fluid containing 15,000 polymorphonuclear cells per cubic millimeter. The spinal fluid protein was 85 mg., the chlorides 670 mg. per hundred cubic centimeters. The sugar was too low to be accurately determined by the ordinary tests. A stained smear of the

From the Surgical Service, U. S. Marine Hospital.

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spinal fluid showed a gram positive diplococcus which morphologically resembled the pneumococcus.

With the signs and symptoms indicative of meningeal infection, the administration of sulfapyridine was begun. Four Gm. of sodium sulfapyridine was given intravenously followed by an additional 2 Gm. in six hours. Subsequently, sulfapyridine was given by mouth in doses of 2 Gm. every four hours for four doses.

At this time (twenty-four hours after onset of signs of meningeal infection) the culture of the spinal fluid was reported as showing a nonhemolytic streptococcus. The sulfapyridine was then discontinued and sulfadiazine was started in doses of 2 Gm. every four hours. After three days the amount of this drug was reduced to 1 Gm. every four hours. The patient was considerably improved, although the temperature remained at 38 C. to 39 C. (100.4 F. to 102.2 F.) and there was still definite rigidity of the neck and positive Kernig signs. Culture of the spinal fluid remained positive. Despite these findings, the patient was rational, oriented and was able to take nourishment and medication orally. The accompanying restlessness, irritability and severe headaches were alleviated greatly by lumbar drainage.

After twelve days of this medication, the patient showed pronounced general improvement and the drug was discontinued. At this time the spinal fluid was clear, the cell count was 110, the dynamics were normal and the culture was negative.

Within seventy-two hours after cessation of the drug the patient began to complain of severe headache and showed increasing restlessness. Sulfadiazine was begun in doses of 1 Gm. every four hours. In twenty-four hours the headache and restlessness had disappeared and the temperature was normal. The drug was continued for eight more days. The patient remained rational and comfortable, with no complaints other than occasional slight headache and very slight rigidity of the neck. There was no recurrence of either the symptoms or the fever. A lumbar puncture done thirty-three days after the onset of the meningitis (ten days after final discontinuance of the drug) showed normal dynamics and clear spinal fluid with normal cell count, sugar, chlorides and total protein and negative culture. There were no psychic changes or neurologic sequelae demonstrable. The patient was discharged from the hospital as recovered on March 25, 1942.

COMMENT

In analyzing this case we believe that the following points are worthy of emphasis.

1. Despite the numerous reports of cases of streptococcic meningitis following otitis successfully treated with the sulfonamides, a review of the literature reveals a comparative rarity of cases following cerebral trauma which have been successfully treated by chemotherapy. To our knowledge this is one of the earliest cases treated with sulfadiazine with recovery.

2. The mortality of streptococcic meningitis, which in the presulfonamide era was almost 100 per cent, has been reduced materially through the introduction of chemotherapy. The minimal toxicity of the newer sulfonamides such as sulfadiazine should lead to a more obvious decline in the mortality rates of these infections.

3. The effectiveness of sulfadiazine as a therapeutic agent coupled with its low toxicity makes this the drug of choice in the treatment of streptococcic meningitis. In this case no single symptom which could be classified as due to toxicity of the drug was noted. There was no nausea or vomiting, no cutaneous eruption, no hematuria, no elevation of the nonprotein nitrogen and no decided change in the blood picture other than a mild secondary anemia, despite the administration of rather large doses for long periods.

Special Article

HANDBOOK OF NUTRITION: XXI

NUTRITIVE REQUIREMENTS IN PREGNANCY AND LACTATION

J. HARRY EBBS, M.D.
TORONTO, ONT.

These special articles on foods and nutrition have been prepared under the auspices of the Council on Foods and Nutrition. The opinions expressed are those of the authors and do not necessarily reflect the opinion of the Council. These articles will be published later as a Handbook of Nutrition.—ED.

The ideal normal nutritional state for pregnancy would be one in which the maternal body was endowed with the proper nutritional elements before, during and after the pregnancy, to ensure the optimum needs of the fetus in its intrauterine development, to supply stores for its needs in early infancy, to ensure adequate nutrition for the normal physiologic requirements of the mother, and for the added requirements resulting from pregnancy and lactation. It is therefore not enough to discuss the question of diet for the expectant mother by simply saying that her needs are those of any healthy woman. While we have been accustomed to thinking of the fetus as parasitic and therefore obtaining its nutritional needs even at the expense of the maternal stores, perhaps we should consider more optimum development of the fetus by making all needs readily available. Gross nutritional deficiencies are seldom encountered in the population today, but, as our knowledge of nutrition increases, more and more evidence is presented that there are minor deficiencies which impair to varying degrees the health and efficiency of our population. Such minor or subclinical deficiencies, which in the average individual would take weeks or months to develop, could be exaggerated and hastened by the increased nutritional needs during pregnancy.

To serve as a basis for discussion of the nutritive factors needed during pregnancy and lactation, without considering special obstetric problems, such as vomiting, it might be well to use table 1, which is a reproduction of the standards set by the Food and Nutrition Board of the National Research Council and adopted by the Washington National Nutrition Conference in May 1941 and by the Council on Foods and Nutrition of the American Medical Association.

DIET DURING NORMAL PREGNANCY

In order to supply the food essentials in the recommended amounts it would be necessary to provide the following foods daily in approximately the amounts specified: milk, 40 ounces (2½ pints); cheese, 1 ounce; butter, 2 ounces; egg, 1 serving; meat, 1 serving (liver once a week); potato, 1 serving; yellow or green leafy vegetable, such as carrots, spinach, chard, string beans, or green peas, 1 serving; vegetable such as cabbage, turnip or tomato, 1 serving; orange juice, 3 ounces, or grapefruit juice, 4 ounces, or tomato juice, 7 ounces; other fruits, 1 serving; whole grain or enriched bread, 4 slices; whole grain or restored cereal, 1 serving. Extra calories necessary would be provided in the other foods

From the Department of Pediatrics, University of Toronto Faculty of Medicine.

eaten in the daily diet according to the individual needs and taste. A supplement of fish liver oil or its equivalent should be prescribed to provide 400 to 800 units of vitamin D.

CALORIES

McCollum [1] states that during pregnancy there is a rise in basal metabolism which is 23 per cent higher at term than at the fourth month. The gain in weight, however, is only 14 per cent. The fetal tissues have a higher specific metabolism per unit of weight than maternal tissues. While there is increased metabolism toward the end of pregnancy, this is to some extent compensated by the necessary restriction of muscular activity during this period. The normal desirable weight gain in pregnancy according to some authorities is 20 to 25 pounds, spaced to gain 3, 10 and 10 pounds in the three trimesters.[2] The appetite is often diminished during the first trimester, and caloric requirements may be difficult to maintain. In the latter half of pregnancy the appetite may be increased.

FAT AND CARBOHYDRATE

Fats and carbohydrates supply the energy in the normal diet and are usually present in sufficient quantity. Their importance apart from being a source of calories, is in the absorption of vitamins by the fat and the protein sparing action of carbohydrate. The ratio of carbohydrate and fat to protein and other so-called protective foods usually varies with the economic level of the family. The lower the income, the lower the intake of animal protein and vitamin containing foods.[3] Obesity and excessive gain of weight during pregnancy can be controlled to a certain degree by the regulation of the intake of fat and carbohydrate.

Rucker [4] feels that a carefully controlled diet will determine the weight of the baby. By keeping a low fluid, fat and carbohydrate intake and by increasing the protein, while keeping the total calories about 1,800 a day, he claims that the length of labor is shortened and that there is a minimum of prematurity. However, most observers feel that only gross curtailment of food intake can affect the size of the fetus. In such cases there is always the danger of some or many specific deficiencies. Garry and Stiven,[5] in a review of the available data up to 1935, find that the weight of the newborn is not influenced by the maternal diet unless there are extreme deficiencies. This has been my experience, in which it was found that the average birth weight of babies born to a group of mothers who were given extra food during the latter months of pregnancy was 7 pounds 7 ounces, compared with an average of 7 pounds 10 ounces in a group whose mothers were left on a poor diet which was much lower in total calories.[6]

PROTEIN

Metabolism studies as reported by several workers [7] indicate the increased requirements for protein during pregnancy and lactation. The needs of the normal nonpregnant woman of about 1 Gm. per kilogram of body weight must be increased to a total of from 90 to 125 Gm. daily in order to provide for the growth of the fetus and the uterus.

The role of protein in kidney damage and its place in the cause and course of toxemia of pregnancy are still debatable.[8] Protein is still restricted by many in the management of toxemia, and it is believed that clinical experience supports the view that toxemia is improved or prevented by protein restriction.

Williams [9] says that a deficiency of protein may lead to nutritional edema and tends to anemia, poor muscle tone, lowered resistance to disease and poor milk supply.

Barker [10] found protein poor diets in about 50 per cent of both clinic and private patients. A condition of edema, sallow pasty complexion and puffiness of the face cleared up when his patients were put on a high protein diet.

An increase in protein in the diet tends to increase the yield of breast milk, while a decrease lowers the quantity of milk secreted.

Coons and Blunt [11] found that, the greater the retention of nitrogen in the last months of pregnancy, the better the chance of successful lactation.

One half of the protein in the diet should come from meat, eggs and dairy products.

TABLE 1.—*Recommended Daily Allowances of Dietary Essentials for Women*

	Calories	Protein, Gm.	Calcium, Gm.	Iron, Mg.	Vitamins A, I. U.	Vitamins B_1, Mg.	Vitamins C, Mg.	Vitamins Riboflavin, Mg.	Vitamins Nicotinic Acid, Mg.	Vitamins D, I. U.
Woman, 56 Kg., nonpregnant...	2,500	60	0.8	12	5,000	1.5	70	2.2	15	0
Pregnancy (latter half).....	2,500	85	1.5	15	6,000	1.8	100	2.5	18	400-800
Lactation.....	3,000	100	2.0	..	8,000	2.3	150	3.0	23	400-800

(Formulated by the Food and Nutrition Board of the National Research Council, 1941.)

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CALCIUM, PHOSPHORUS AND VITAMIN D

One of the most important elements of the diet during pregnancy and lactation is calcium. With this mineral one can also link phosphorus and vitamin D. A decrease in the serum calcium in the last months of pregnancy has been shown,[12] with a return to normal after the pregnancy has terminated. In successive pregnancies with only short periods between, the serum calcium has been shown to be even lower. Mendenhall and Drake [13] have ascribed numerous symptoms and complaints to a lack of calcium during pregnancy. They cleared up such complaints as muscle soreness, spasms, numbness, tingling and neuritis by giving calcium and viosterol to these patients.

Swanson and Iob,[14] in a chemical analysis of the fetus, have shown that the calcium and phosphorus retained in the last two lunar months is 65 and 64 per cent respectively of the total body content of the full term fetus. In order to supply these needs, a daily intake of 1.5 to 2.0 Gm. of calcium is necessary.[15]

The relationship between calcium, phosphorus and vitamin D has been the subject of much research. It seems clear that vitamin D is related to the utilization and retention of calcium and phosphorus in the body. Vitamin D requires an adequate supply of calcium and phosphorus in order to provide a retention. In rats vitamin D causes an increased retention of calcium and phosphorus in the offspring when the diet is adequate.[16] In a review by Jeans and Stearns [17] it is pointed out that some persons can retain calcium in ample amounts if the intake is from 1.6 to 2.5 Gm., even without added vitamin D, but in rapidly succeeding pregnancies and periods of lactation, unless vitamin D is given there may be poor retention of calcium and phosphorus regardless of the intake.

That the amount of calcium and vitamin D in the mother's diet affects the density of the infant's bones and the structure of the teeth has been observed.[18] Evidence has been presented to show the relation of the maternal diet to the development of rickets in the offspring. Maxwell [19] has reported fetal rickets. Mellanby [20] has stated that calcium and vitamin D are often deficient in the mother's diet and feels that this is one of the predisposing factors in the development of rickets, Grant and Goettsch [21] have shown a greater and earlier tendency to rickets in rats born of mothers on diets low in calcium, phosphorus and vitamin D.

Macy and her co-authors [22] reported that the addition of cod liver oil and yeast to the diets of nursing mothers resulted in improved calcium assimilation and a greater feeling of well being.

The amount of vitamin D which is necessary for adult mineral metabolism is not definitely known and the amount suggested in table 1, of 400-800 units, is largely arbitrary. The administration of vitamin D in some form seems to be indicated.

In supplying the calcium in the food, the requirements for phosphorus are usually automatically supplied.

IRON

A great deal of interesting work has been published in the past few years which has given us a clearer understanding of the relation of the maternal diet to the development of anemia in the mother and the infant. Studies in the anemia of rats have done much to help in the understanding of anemia in the human infant. Parsons, Hickmans and Finch [23] showed that rats fed on an iron deficient diet can rear their litters, but the second generation fed on the same diet will have diminished reproductive ability, the young will not grow properly and they will show a pronounced anemia. The hemoglobin at birth is lower in the second litter of rats on an iron deficient diet.[24] Murphy and Bowes [25] found that anemia was twice as frequent among mothers using an inadequate diet as among those using an adequate diet. Once the anemia is established, whether the so-called physiologic anemia of pregnancy or an iron deficient anemia, it is then impossible to raise the level by diet, no matter how nourishing or how much iron is available. It is therefore necessary to provide iron in such cases. Both maternal anemia and anemia of infants can be prevented by prophylactic iron therapy. Labate,[26] in studying three groups of women on different diets, reported that iron increased the hemoglobin whether the diet was good or not.

Neale and Hawksley [27] give as the cause of anemia in the mother (1) transfer of maternal reserve to fetus, (2) poor diet, (3) rapidly repeated pregnancies and twin pregnancies and (4) gastric anacidity or hypoacidity. The cause of anemia in the infant, according to Parsons and Hawksley,[28] is either a deficient ante-

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natal storage of iron or a deficient postnatal supply, or both. A prime factor in this deficiency is the presence of anemia in the mother. Strauss [29] pointed out that anemia was present during the first year of life in babies born of anemic mothers although the hemoglobin was normal at birth. Mackay [30] showed that there was a lower level of hemoglobin in every month of the first six months of life in infants born of anemic mothers than in infants born of mothers without anemia.

The minimum requirement during pregnancy seems to be 15 mg., and according to Macy and Hunscher [31] it may be 20 mg. daily. Corrigan and Strauss [32] showed the value of supplementing the antepartum diet with medicinal iron. The results obtained in the blood of the mothers were equally striking in the blood of infants in similar studies by Gottlieb and Strean.[33]

VITAMIN A

The daily requirement of vitamin A is as yet unknown, but, from various surveys and as a result of correlated dark adaptation tests, suggested requirements have been set forth. That these are far from being completely acceptable is seen when one considers the difficulties and discrepancies in the methods of measurement. The manifestation of vitamin A deficiency in any gross form is extremely rare. The incidence of minor or subclinical deficiencies is as yet unknown, but newer methods of detection may bring these to light in the near future. Again, the widespread distribution of vitamin A and its precursor carotene in our common foods suggests that it is probably not seriously deficient. However, pregnancy and lactation place extra demands on the normal physiologic processes of the female, and it is probably wise to aim at an optimum level of vitamin A and thus be within the margin of safety until our present knowledge of requirements is extended.

The part played by vitamin A in reproduction is uncertain. Mason [34] noted an increased rate of premature births and stillbirths in animals on vitamin A deficient diets. The young were not suckled as long and lived a shorter time than normal. On the other hand, Cannon [35] found that congenital anomalies were not induced in the young of rats with a lack of vitamin A in the diet. They did, however, show abnormalities of pregnancy and labor as well as a tendency to sterility.

Williams, Hark and Fralin,[36] in observing a group of pregnant women, found 62 per cent with a low vitamin A content in an analysis of their dietary records. Only 37.5 per cent of these women had poor dark adaptation. Hirst and Shoemaker [37] found no significant obstetric complications among the women with vitamin A deficiencies.

Ricketts [38] has described severe deficiency manifestations of vitamin A simulating toxemia of pregnancy. His report deals with 2 cases.

The role of vitamin A in the development of the fetus and therefore its importance in pregnancy is strongly suggested by the work of Wolbach and Howe.[39] They have shown changes in the structure of the developing teeth in vitamin A deficient rats and guinea pigs. Mellanby [40] has shown defective teeth in rats born of mothers on a diet deficient in vitamin A and feels that vitamin A deficiency is responsible for absent or defective enamel and dentin.

While the newborn infant has very low stores of vitamin A,[41] the colostrum and early human milk are rich in this vitamin. Human milk contains the same amount of carotene and vitamin A as cow's milk but at the beginning of lactation contains five to ten times more.

It seems safe in our present knowledge of vitamin A requirements to believe that the requirements during pregnancy and lactation will be met by diet and the same supplement which provides vitamin D, namely 4 to 6 Gm. of cod liver oil or its equivalent.

VITAMIN B COMPLEX

Cowgill [42] has shown that the requirement of the average person for vitamin B_1 depends on the basal metabolism and the caloric intake. Since these are increased in pregnancy and lactation, the intake of vitamin B_1, or thiamine, must be increased. Polyneuritis can occur during pregnancy,[43] and signs of minor deficiencies of vitamin B_1 are not uncommon. We [44] have been impressed by the changes which occurred when the intake of vitamin B_1 was doubled or trebled in women attending the antepartum clinic who had been on poor diets. Many of the minor aches and pains and numerous complaints disappeared. The mental attitude of many of these patients changed from one of apathy and discontent to one of interest in the outcome of their pregnancy. Williams and his co-workers,[45] in a nutrition study of pregnant women, found practically one third of their patients on an inadequate intake of vitamin B_1, according to the Cowgill standard. Thirty per cent of those with an inadequate intake had moderate to pronounced nausea and vomiting compared with only 10 per cent of those with an adequate intake. Fatigue, cramps, paresthesias and dyspnea were also found more frequently in those with a low vitamin B_1 intake. Strauss and McDonald [46] point out that such evidences of polyneuritis should be treated with vitamin B complex.

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The need of the lactating woman for vitamin B_1 is obviously higher than for the normal nonlactating woman. Cowgill [47] sets this at 15 or 20 units per hundred calories, which would be 500 to 700 units daily. The amount of vitamin B_1 in the milk depends to some extent on the amount in the mother's diet.[48] There is practically no storage of this vitamin in the body. The stimulating action of B_1 on the secretion of milk has been observed.

Riboflavin, or vitamin B_2 (G), is associated with oxidation processes of the cell. With the increased metabolism during pregnancy, the requirement of this vitamin is probably increased. Forms of keratitis have been described as evidence of deficiency of this vitamin.[49] The condition described by Sebrell and Butler [50] as a result of deficiency of riboflavin has been observed in 1 patient in our own clinic.

Riboflavin is found in milk, egg white, liver and leafy vegetables in such proportions that most diets should contain a sufficient amount.

Nicotinic acid and vitamin B_6 have not been demonstrated as having any particular significance during pregnancy, except that the requirement is probably increased in proportion to those of the other vitamins.

If the diet contains an adequate amount of whole grain products, milk, meat, egg and vegetable, the components of the vitamin B complex will be supplied in sufficient amounts.

VITAMIN C

With the perfection of methods for determining vitamin C in the body, the approximate needs have been fairly clearly determined for the average woman during pregnancy and lactation. Snelling and Jackson [51] in this clinic found a slight fall in the ascorbic acid level of the blood plasma toward the end of pregnancy. This and a further drop during and after labor might be explained by the decreased intake at this time and by increased needs of the fetus.

Being water soluble, vitamin C is not retained in the body and therefore the level in the blood is directly affected by the amount in the diet.[52]

The average plasma vitamin C of two groups of women measured during pregnancy is shown in table 2. Both groups were on poor diets when the blood was first examined. One group was then given one orange and 4½ ounces of canned tomatoes daily until the end of pregnancy. It will be noted that the average level of ascorbic acid in this group was higher in the eighth month and at term than in the other group. The parasitic nature of the fetus is demonstrated by the average level of vitamin C in the cord blood, which is higher than the level in the maternal blood at this time. Even when the maternal blood was practically depleted of ascorbic acid, the cord blood would contain appreciable though below normal amounts. The average levels in table 2 are lower than the desired level during pregnancy.

Sellig and King [53] have shown that the amount of vitamin C in the breast milk is dependent on the dietary intake of the mother. Totally breast fed babies are well supplied with vitamin C if the vitamin C content of breast milk is more than 4 mg. per hundred cubic centimeters. Mothers on low vitamin C diets can secrete enough vitamin C in the breast milk to give levels in the plasma of the infant which are higher than their own. While cases of scurvy in breast fed infants have been known, it is an extremely rare occurrence. Of 20 consecutive babies with scurvy admitted to the Hospital for Sick Children, Toronto, all were bottle fed.

It seems clear that the vitamin C intake during pregnancy and lactation should be increased above the amount usually required. Particular attention should be paid to the intake during the latter weeks of pregnancy, during lactation and during periods of vomiting or other dietary restriction. The diet should contain liberal amounts of orange, grapefruit or tomato juice as well as other fruits and vegetables.

TABLE 2.—*Plasma Vitamin C During Pregnancy*

Group	5th to 6th Month Mg. per 100 Cc.	8th Month Mg. per 100 Cc.	Term Mg. per 100 Cc.	Cord Blood Mg. per 100 Cc.	Mother's Blood 6 Weeks After Delivery Mg. per 100 Cc.
Diet poor in vitamin C	0.47	0.40	0.47	1.0	0.43
Improved diet; added orange and tomato	0.46	0.69	0.73	1.4	0.38

VITAMIN E (ALPHA-TOCOPHEROL)

The need for vitamin E in normal pregnancy has been suggested recently. Its widespread distribution in foodstuffs makes it unlikely that any serious deficiency can occur. Reports of Vogt-Møller,[54] Currie,[55] Shute,[56] Collins [57] and Watson [58] on the use of wheat germ oil in habitual abortion have been very encouraging. Further reports continue to appear. Bacharach [59] summarizes the recent reports by suggesting that there is at least presumptive evidence that it is needed for normal pregnancy in women.

VITAMIN K

Evidence has been brought forward practically to establish the usefulness of vitamin K.[60] The administration of this substance to the mother just before the onset of labor or, failing this, during labor has a definite effect on the prothrombin time of the infant.[61] A reduction in the incidence of hemorrhagic disease in the newborn period has been shown when mothers have been treated, and the use of this substance also seems to be indicated in the treatment of cases of hemorrhagic disease of the newborn.[62]

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RELATION OF NUTRITION TO TEETH

Studies of the incidence and control of dental caries in the pregnant woman indicate that diet is a factor. There appears to be some truth in the old saying "For every child a tooth," and the observation has been commonly made that dental decay is increased during pregnancy.

The teeth, while requiring relatively little mineral salts in comparison to the skeleton, are nevertheless dependent on maternal supplies for their normal development. Deficiencies in the maternal stores of essential food elements, such as minerals and vitamins, will probably be reflected in the structure of the teeth of the infant. Toverud [63] has found defects in the teeth under such conditions, and Mellanby [64] feels that deficiencies in antepartum diet are an important factor in dental caries appearing in the child.

In observations on three groups of patients in an antepartum clinic Daro [65] found a poorer condition of the teeth and gums in those who were on inadequate diets compared to those who were eating plenty of milk, raw fruits and vegetables. He points out the importance of deficiencies which might occur as the result of vomiting early in pregnancy.

Howe [66] makes a strong point: "The dentist may and should indicate to the medical practitioner that the teeth are calcifying and the bones which carry the teeth are undergoing ossification during fetal life, and it is his duty to see that the normal processes of growth and development here go on uninterrupted. It is recognized that these processes are influenced more strongly by nutritional states than by any other factor."

While there are undoubtedly other factors in the production of dental caries, it seems reasonable that the period of development of the teeth is a most important one and the mother should be provided with the optimum requirements.

NUTRITION A FACTOR IN PREGNANCY

Is nutrition a factor of importance in the management of pregnancy? This question could be answered by general statements covering the knowledge that improved nutrition improves the general health and this results in healthier mothers. Common sense and practical experience suggest the importance of proper food for the expectant mother. Poverty goes hand in hand with poor diets, but not all people with adequate incomes provide proper diets. Ignorance, illness and other circumstances also interfere with proper dietary habits.

The incidence of successful pregnancies is conceded to be better in those of good or moderate means in comparison to those who are on low income. A recent communication by Baird and Wyper [67] from Aberdeen makes such a comparison. In private specialist practice the rate for stillbirths and neonatal deaths was 12 per thousand, in hospital practice it was 54.5 per thousand and in the homes it was 78.5 per thousand live births. While there are several probable factors entering the outcome of these three classes of pregnant women, such as economic, nursing and medical, the authors say "There is thus a large wastage of child life associated with childbirth in Scotland, intimately connected with unfavorable economic conditions and malnutrition and fatigue in the mother."

Ross and his associates [68] reported that, in two groups of pregnant women, one group on a poor diet and another group on a well balanced diet, the incidence of toxemia and the levels of hemoglobin and serum protein were not significantly different. Church, Foster and Asher [69] showed that the diet of the mother was a factor in the survival of the offspring from the risks of infection.

In a recent study in this clinic [70] a group of pregnant women found to have very poor diets were divided into two groups. One group of 120 women on poor diets and with low incomes were followed during the last half of pregnancy as controls for 90 women on equally poor diets and low incomes who were supplied with milk, eggs, cheese, oranges, canned tomatoes, wheat germ and vitamin D capsules and who were instructed in the type of diet necessary for pregnancy. The observations made throughout pregnancy, during convalescence and on the baby showed a striking difference. The incidence of miscarriages, premature births and stillbirths, the number of infections in the mother and her general condition, both mental and physical, were much better in those who received the extra food. Changes in the blood of the mothers given extra food gave evidence that they were in a better condition during the stress of pregnancy. The general condition of the babies born of mothers who received the extra food was much better than the condition of those born of mothers who were left on their poor diets. The incidence of illness among the babies was much greater in the poor diet group.

While it is well recognized that there are many factors in the successful outcome of pregnancy, it seems reasonable that proper nutrition will ensure a more optimum general condition of the mother which will possibly prevent or at least minimize the complications that occur in pregnancy. The tired, depressed and physically poor women in this study, with a past history of a high percentage of complications, were poor obstetric risks. But even in four or five months of proper feeding this condition was greatly improved and the outcome of pregnancy was not only better than with those who were left on their poor diet but resulted in a lower rate of complications than they had experienced in previous pregnancies. This series is small and should be extended in women equally poor.

A much larger experiment was conducted in Great Britain,[71] and, while the results were obtained in several districts and the experiment was not confined to one hospital, the series is so large and the results are so striking that they have some significance. Milk and egg products containing added vitamins A and D and another food rich in vitamin B were supplied during the last three months of pregnancy to needy mothers in the special areas of England and South Wales. The maternal death rate in 10,384 obstetric cases in which these foods were supplied was 1.66 per thousand total births as against a rate of 6.15 among 18,854 other cases in the same districts during the same period. There

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was only one death from sepsis in the assisted group, as against forty-five in the nonassisted group. The number of stillbirths and neonatal deaths was 43 per cent less in the experimental group than in the nonassisted category.

SUMMARY

From the evidence presented it is apparent that the pregnant and lactating woman requires more calories, minerals, vitamins and protein than the nonpregnant woman. As shown by McCance and his associates [72] the intake of these elements is influenced by the economic level in that "a rise in spending power led to an increased consumption of milk, fruit, vegetables and meat and a decreased consumption of bread and total cereals." They found the women on the better diets to be taller and less anemic.

The management of the nutritional needs of the expectant mother requires more care in the selection of a daily diet than does that of a normal nonpregnant woman. The increased requirements for protein, minerals and vitamins, if they are to be met by the food consumed, necessitate some instruction in most cases. This instruction can be given by the physician or by the dietitian in the clinic. Simple directions stressing the importance of eating the foods which supply the greatest amounts of the protective food elements are usually sufficient. The importance of milk, citrus fruits, green and yellow vegetables and whole grain bread and cereal are obvious. Apart from vitamin D, the requirements for the other food elements can be met by the food, provided the income is adequate.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

VIBRAPHONE NOT ACCEPTABLE

Manufacturer: European Vibraphone Company, 120 Wigmore Street, London, W. I. American Representatives, European Vibraphone Company, Inc., 4687 Hollywood Boulevard, Los Angeles.

The following description of the Vibraphone has been taken from the advertising used to promote the device:

"The Vibraphone is a tiny hollow instrument made of pure silver. A minute silver shell, within which is a vibration chamber, acts as a receiver of sound. . . . It fits snugly into your ear. The tube of the instrument going into the opening of your ear until the ball settles comfortably into position. The shell, or vibration chamber rests in the curve of the outer ear. There are no wires, no batteries, nothing electric and there are no head bands, no trumpets, nothing to fit behind the ear, or to carry in the pocket or handbag."

In the firm's advertising is the following description of how the Vibraphone will aid the deafened person to hear:

"This principle is a valuable development of science. When sounds enter the Vibraphone a strong vibration is set up which transmits the sound impulses to the inner ear. With daily use, the affected ear accustoms itself to this helpful stimulation, and normal sounds may be heard with natural clarity in many cases.

"The remarkable quality of these sound waves from the Vibraphone lies in the fact that they tend to set up vibrations in affected ears which normally have lessened power to transmit sound to the brain. Ears which are too sluggish, ears which have become out of order, and partially deaf by reason of causes already mentioned, tend to liven up under the continuous 'massage' of this amplified and concentrated sound from the Vibraphone. Hearing functions gradually tend to waken into activity and your ear begins to live once more. Improved hearing is evidence of this.

"The progress of the improvements is more evidence still. Time will tell how perfect your hearing may become. The fact that your hearing is improved shows that your deafness may be bettered. Your confidence is justified. Your patience is rewarded."

The theory of "gradually massaging the organs back to sensitiveness" by means of vibration has been exploited in other instances, and in no case has any critical evidence been submitted to substantiate it. The manufacturer of the Vibraphone asks the purchaser to withhold judgment of the "aid" until it has been used several weeks.

According to a statement, "Your Deposit is Insured," in the promotional material, ". . . said European Vibraphone Company, Inc., warrants in its customers contract to refund to the purchaser of its Vibraphone products the purchase price thereof, less service charge of Six and no/100 Dollars ($6.00) per pair or Three and no/100 Dollars ($3.00) on a single Vibraphone if such product be found not satisfactory during the thirty (30) day trial period offered." This financial arrangement seems to be very advantageous to the firm. Even though the customer has derived no benefit from the device and returns it he pays enough for the privilege of trying it. The manufacturer thus collects the "service charge" and also receives the instrument, which he may resell.

It is not known whether the Vibraphone now promoted by the European Vibraphone Company and the Vibraphone referred to in the following paragraph are one and the same instrument, but the claims made for the two instruments are identical and photographs of the devices show them to be very similar in appearance.

According to the article "Deafness Cure Quackery and Pseudo-Medicine" by Dr. Arthur J. Cramp, former director of the Bureau of Investigation of the American Medical Association (*Hygeia* **4**:21 [Jan.] 1926), the Vibraphone is an offspring of the "Radium Ear" or "Audiophone" device promoted by one Charles Fensky. The Fensky device was a similarly shaped instrument which was "improved" by the addition of a "vibrator." A St. Louis firm, the Vibraphone Company, took over promotion of the instrument.

The Better Business Bureau sent out a report on the Vibraphone in 1929 in which the results of an investigation made by the bureau were given. Several hundred letters were written to persons said by the manufacturer to be satisfied users of the instrument. By far the majority of the replies indicated that the device had been of no value as an aid to hearing. Many said that they could not wear it because it was so uncomfortable.

No evidence that this device, when tried under controlled conditions, would amplify sound and improve the hearing of a deafened person was made available. The Council voted not to include the Vibraphone in its list of accepted devices.

ALLERGEN-PROOF ENCASINGS ACCEPTABLE

Manufacturer: Allergen-Proof Encasings, Inc., 4060 Superior Avenue, Cleveland.

The Allergen-Proof Encasings were declared acceptable for inclusion in the Council's list of accepted devices in THE JOURNAL of March 20, 1937, page 972. Designed to protect persons allergic to dust, feathers, cottonseed or kapok, the covers (fitted for various sized mattresses, pillows and box springs) were made of a rubber fabric composition treated by a process which increased the resistance of rubber to oxidation.

Because of priority restrictions the manufacturer is now unable to obtain a supply of the original fabric. A substitute has been found by the firm. This material is a cotton fabric impregnated with pyroxylin. According to the Council tests the material stands washing and ironing as claimed by the firm. It was tested against the effects of dilute acids, alkali and soap. It stands up fairly well but is not as satisfactory as the original material. The Council believes it to be as good as can be obtained at the present time and that it will give satisfactory service if the manufacturers' directions are followed.

The Council voted to retain the Allergen-Proof Encasings on its list of accepted devices.

72. McCance, R. A.; Widdowson, E. M., and Verdon-Roe, C. M.: A Study of English Diets by the Individual Method: III. Pregnant Women at Different Economic Levels, J. Hyg. **38**: 596-622 (Sept.) 1938.

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SATURDAY, JANUARY 30, 1943

POSTOPERATIVE NITROGEN LOSS

Much of the tremendous advance in surgery in the past decade or more has been achieved because of the recognition of various biochemical deficiencies and their correction by appropriate replacement therapy. Loss of water, loss of electrolyte, loss of plasma have all been studied and now are corrected rapidly and effectively by the parenteral route. Indeed, with the purification of vitamins, many of them can also be administered parenterally and replacement therapy carried out along with the intravenous injection of saline solution, dextrose and plasma.

Nitrogen loss after operation has been largely overlooked even though such loss, unless replaced immediately, means depletion of tissue protein. More important, the loss leads to hypoproteinemia, which, if severe, produces many serious clinical manifestations. Especially significant, therefore, are the recent studies of Brunschwig and his co-workers[1] at the University of Chicago. They observed the nitrogen loss by 41 patients who were operated on for various reasons; the results were given in three groups and averaged 2.5, 5.1 and 8.9 Gm. daily. The greatest loss was by a patient who had had a gastric resection and who, during ten days after operation, was unable to take food and lost 175 Gm. of nitrogen. This figure represented his negative balance and corresponds to 1,100 Gm. of protein, which actually means 5,500 Gm. of tissue protein. In other words, this patient lost, during his first ten postoperative days, over 12 pounds of muscle tissue or its equivalent. The significance of this loss, however, lies not in the loss of muscle tissue, for after all voluntary muscle is not needed for an immobile patient at rest in bed. The important point to emphasize is that all protein tissues of the body are affected, even though in varying degrees. Of these, plasma protein is of primary importance and postoperative hypoproteinemia has in fact been amply observed by many surgeons; of these perhaps one of the earliest was that of Jones and Eaton.[2] Doubtless with further study other manifestations of this excessive loss of nitrogen will become known. For example, depletion of liver protein provokes or at least aggravates the possibility of hepatic insufficiency, particularly when disease of the liver is present or is developing. Significant too, as indicating a deficiency, are the observations of Farr and his co-workers,[3] who found a fall in the amino acid nitrogen of the plasma during general anesthesia, which proceeded to an even lower level after operation.

Other observations[4] on the tremendous loss of nitrogen following trauma, burns and operations amply justify the implications which flow from the Billings Hospital study. For example, it was obviously impossible to correct this loss by the usual methods of therapy. Oral alimentation helped, but after abdominal operations eating is often contraindicated and in many instances was in any event limited because of anorexia. Intravenous dextrose spared protein breakdown and reduced nitrogen loss to a considerable extent but could do so only by supplying adequate calories; unfortunately the loss of nitrogen is only in part due to this factor. Plasma transfusions are useful but, for the small amount of protein food introduced, are expensive and inconvenient. Actually the loss was corrected by supplying nitrogen in the form of the building stones of protein (amino acids and polypeptides), which were prepared from a digest of casein and pork pancreas and injected intravenously, thus achieving a physiologic short cut over the natural method by sparing the need for digestion and absorption in the gastrointestinal tract. In many of the cases a sufficient dose was injected so that positive nitrogen balance was achieved. One patient with an obstruction of the sigmoid took nothing by mouth, yet 50.8 Gm. of nitrogen was retained during ten days or, in terms of muscle tissue, a gain of nearly 3½ pounds. In others the magnitude of the protein depletion was significantly lowered. The importance of dextrose in the metabolism of amino acids was shown by the failure to achieve nitrogen balance with the protein digest alone. Other observers also have used intravenous injections of hydrolyzed protein and have confirmed these results.[5]

It may be pertinent now to emphasize the importance of covering postoperative loss of nitrogen in this way as a routine. Dextrose is widely given after operation to supply calories, yet nonessential tissue fat can easily substitute in part for it; nitrogen loss, on the other hand, must be met by exogenous sources unless

1. Brunschwig, Alexander; Clark, D. E., and Corbin, Nancy: Ann. Surg. **115**: 1091 (June) 1942.

2. Jones, C. M., and Eaton, Frances B.: Postoperative Nutritional Edema. Arch. Surg. **27**: 159 (July) 1933.

3. Farr, L. E., and others: Proc. Soc. Exper. Biol. & Med. **50**: 256, 1942.

4. Cuthbertson, D. P.: Lancet **1**: 433 (April 11) 1942. Lucido, Joseph: Ann. Surg. **111**: 640 (April) 1940. Elman.[5]

5. Elman, Robert: Ann. Surg. **112**: 594 (Oct.) 1940. Gardner, C. E., Jr., and Trent, J. C.: Surg., Gynec. & Obst. **75**: 657, 1942.

depletion of essential body and plasma protein is to be avoided. In this sense consideration of nitrogen loss after operation deserves more serious consideration than caloric needs. This is particularly true in view of the ease and simplicity with which the loss can now be covered. The intravenous injection of protein nourishment with protein digests is certainly now as convenient as the administration of dextrose and saline solution; this contrasts strikingly with the inconvenience and expense of giving large transfusions of plasma as a source of protein food. Many hitherto unexplained postoperative complications are undoubtedly due to excessive nitrogen loss and will be avoided by extensive use of this new method of parenteral protein alimentation.

ADVANCES IN MUSCLE PHYSIOLOGY

One of the unsolved problems of muscle contraction has been the bridging of the gap between the chemistry of the energy producing reactions involved and the physical processes of shortening and lengthening of the muscle fiber. The detailed chemical transformations of the energy producing mechanisms and their interrelationships have been elucidated during the course of the past two decades, and the energy changes involved have been measured quantitatively. The phosphorylation cycles whereby energy is transferred from carbohydrate breakdown to the muscle fiber have been worked out in detail.[1] Physical studies, chiefly with the aid of x-ray analysis, have yielded a rather complete picture of the alterations which occur in the muscle fiber when subjected to varying amounts of tension in vitro. Muscle contractibility is essentially a molecular contractility of the protein (myosin) chains.[2] However, the means by which the energy produced by the chemical processes is linked or transferred to the muscle fiber so that the latter may actively shorten and relax has been entirely a matter of speculation. Now experiments have been presented which yield data for partial solution of this problem. The story promises to be one of the great contributions of biochemistry to modern medicine.

This important contribution to the integration of the chemical and the mechanical features of muscle contraction has come from a laboratory in the Soviet Union. Englehardt and Ljubimova [3] in 1939 discovered that the enzyme adenylpyrophosphatase is either myosin itself or some closely associated protein. This observation has been confirmed and extended in three other laboratories.[4] Its significance is twofold: 1. The breakdown of adenylpyrophosphate is, of the various processes occurring in the metabolism of muscle, the nearest in time to the contraction of the muscle fibrils. 2. The quantitatively largest part of the breakdown of adenylpyrophosphate probably occurs by splitting off of free phosphate under the influence of the enzyme adenylpyrophosphate, now suggested to be identical with myosin.

The acceptance of the foregoing suggestion rests at present on the failure of all attempts to separate the enzyme adenylpyrophosphatase from the protein myosin. In addition, important supporting evidence comes from detailed observations now available on the physical alterations which occur in the protein myosin as an accompaniment to the combination of myosin with adenylpyrophosphate (enzyme-substrate combination) and the subsequent enzyme action (splitting of inorganic phosphate from the adenylpyrophosphate). Engleharđt and his colleagues [5] treated partially dried myosin fibers, still retaining some adenylpyrophosphatase activity, with a variety of substances. Only adenylpyrophosphate showed any effect, and this was to produce an increase in extensibility of the fibers. Needham and his collaborators [6] have demonstrated that adenylpyrophosphate has a direct influence on the relative optical anisometry and on the shape of myosin particles. The physical changes which take place in the myosin fiber, and the capacity of the latter to catalyze the breakdown of adenyltriphosphate to adenyldiphosphate, are catalyzed by the calcium ion. The importance of the latter ion in maintaining the response of isolated muscle to stimulation has been known from the earliest studies in muscle physiology.

From the available data, a number of interesting concepts are suggested. The essential feature of excitation and contraction in muscle may be, as Bailey [7] has proposed, the liberation of the calcium ion in the vicinity of the adenylpyrophosphate grouping, which can thus, by the almost instantaneous catalysis of adenylpyrophosphate breakdown, make available a large amount of energy. The contraction of the myosin fiber would accompany the combination of the adenylpyrophosphate with the enzyme myosin, as indicated not only by the far reaching changes in myosin observed optically and accompanying the enzyme-substrate combination but also by the enzyme action itself. With this concept the energy producing phosphorylation cycles become coupled with the physical changes in the myosin fiber observable during shortening and lengthening. Indeed, myosin now becomes a "contractile enzyme." One may view the muscle of the body, comprising approximately 25 per cent of the total body weight, as a collection of enzymes.

1. Parnas, J. K.: Ergebn. d. Enzymforsch. **6:** 57, 1937. Needham, D. M.: Enzymologia **5:** 158, 1938.
2. Astbury, W. T.: Ann. Rev. Biochem. **8:** 113, 1939. Astbury, W. T., and Dickinson, S.: Proc. Roy. Soc., series B **129:** 307, 1940.
3. Englehardt, W. A., and Ljubimova, M. N.: Nature **144:** 668 (Oct. 14) 1939; Biochemia **4:** 716, 1939.
4. Szent-Györgyi, Albert, and Banga, I.: Science **93:** 158 (Feb. 14) 1941. Needham, Dorothy M.: Biochem. J. **36:** 113 (Feb.) 1942. Bailey.[7]
5. Englehardt, W. A.; Ljubimova, M. N., and Meitina, R. A.: C. R. Acad. Sc. (U. S. S. R.) **30:** 644, 1941.
6. Needham, Joseph; Shen, Shih-Chang; Needham, Dorothy M., and Lawrence, A. S. C.: Nature **147:** 766 (June 21) 1941. Needham, Joseph; Kleinzeller, Arnošt; Miall, Margaret; Dainty, Mary; Needham, Dorothy M., and Lawrence, A. S. C., ibid. **150:** 46 (July 11) 1942.
7. Bailey, Kenneth: Biochem. J. **36:** 121 (Feb.) 1942.

PREDETERMINATION OF SEX

From earliest antiquity scientists, philosophers and magicians have speculated as to why the offspring is male or female. Biologists have attempted to discover means by which the desired sex could be produced at will. Only with the advent of this century, however, has any scientific foundation for this eventuality been developed. Among the most important early observations was the demonstration that sex among higher animals is determined by genes. Thereafter it became clear that sex is determined in human beings (as in some lower animals) at the time of the fertilization of the egg. Subsequent activity, whether dietary or metabolic, does not change the sex of the child. Furthermore, to the astonishment and possibly distress of some of those with preconceived ideas, human sex is determined by the presence or absence of a particular gene or set of genes of the father rather than by the mother. No longer may the wife be blamed for failure to produce the wished for son!

With the ground work thus laid for scientific approach to predetermination of sex, the subject is emerging from folklore into science. In predetermination of sex of insects and possibly mammals, extensive advances have been made. Gowen and Nelson[1] say that "many problems of sex differentiation and distribution are, of course, left, but, in the sense of establishing means for sex control through specific agencies under man's guidance, the problem of the predetermination of sex may be said to be solved."

The work on which much of this astounding assertion is based has been done by many investigators and is based largely on observations on Drosophila melanogaster—a fly which has served geneticists as the perfect laboratory animal. As Gowen and Nelson point out, the unbalanced condition of one or more chromosome pairs in one sex furnishes the mechanism whereby the distribution of sex in a population is random with a mean approximating an equality for the two sexes. The occurrence of sex linked lethals (a type of gene which results in death and which occurs spontaneously or can be produced by x-rays and other means) gave students of inheritance the first positive means of controlling the sex of the progeny of a set of parents. By refinements of technic involving the introduction of one or more lethal genes in each of the sex chromosomes with prevention of crossing over (i. e. prevention of exchange of genes between homologous chromosomes) it was shown that sex control could be be made practically perfect, with no males to 100 per cent adult females. As the final step in the voluntary control of sex determination, Gowen and Nelson presented an example of genotypic control (control of genetic type) which led to progeny of 100 per cent males. In crosses intended for certain other genetic studies a pair mating of Drosophila melanogaster was observed which produced 136 males and no females. The male progeny of this cross were able to transmit the male producing characteristic to certain of their daughters without regard to the characteristics of the mates to which they were bred. In something over five hundred matings covering a period of eight generations from the original parents, failures in finding the expected male producing genotype did not occur. The daughters with the genotype for all male progeny produced all male offspring without regard to the mates with which they were bred. The males, however, gave no phenotypic expression (i. e. no visible expression) of this inheritance. The male producing genotype is thus without effect on the adult males which carry it. The inheritance is therefore sex limited in its action, affecting only the females which have it, acting as a dominant. This, Gowen and Nelson believe, is the final proof that genotypes may be established which can be genetically controlled for the most divergent sex ratios possible: 100 per cent female in one progeny and 100 per cent male in the other.

This startling discovery does not of course signify that it will be possible in the foreseeable future for parents to choose in advance the sex of their children. But it does establish for the first time on a scientific basis the fact that this can be done experimentally among lower animals by man devised methods.

1. Gowen, John W., and Nelson, Ronald H.: Predetermination of Sex, Science **96**: 558 (Dec. 18) 1942.

Current Comment

PORTS OF ENTRY OF POLIOMYELITIS

Despite much clinical and experimental work, the usual port of entry of poliomyelitis virus has not been precisely determined. The accumulated evidence suggests that the olfactory system is not as a rule primarily involved and that invasion generally occurs through the alimentary tract. The part of the canal most vulnerable to virus penetration, however, is still undetermined. New experimental evidence developed by Faber and his colleagues[1] suggests that the oropharyngeal surfaces are the commonest port of entry. Using cynomolgus monkeys and Sabin's "Per" strain of the virus, the Stanford clinicians were unable to infect monkeys by oral administration of massive doses enclosed in capsules covered with a digestible fat. The same monkeys resisted infection by a high enema consisting of 5 cc. of a 20 per cent virus suspension. Some months later, after zinc sulfate olfactory blockade, the mouth of one of these monkeys was sprayed on three successive days with 5 cc. of a 10 per cent cord suspension supernate. Five days after the first spraying, fever, slight weakness of the arms and mild head tremors were noted, the usual symptoms of incipient poliomyelitis. At this stage the animal was etherized, exsanguinated and perfused with isotonic solution of sodium chloride and 10 per cent solution of formaldehyde. Careful microscopic study was made of the

1. Faber, H. K., and Silberberg, R. J.: Science **96**: 473 (Nov. 20) 1942.

central and peripheral nervous system. Typical lesions of poliomyelitis consisting of small cell infiltrations, chromatolysis, neuronal necrosis and neuronophagia were noted in several ganglions, the heaviest lesions being in both gasserian and in both nodose (tenth nerve) ganglions. Moderately severe lesions were noted in both petrosal (ninth nerve) ganglions, in three of six cervical sympathetic and in two of ten upper thoracic ganglions. Small lesions, few in number, were found in one geniculate (seventh nerve) ganglion, in one lumbar sympathetic ganglion and in two of fourteen thoracic spinal ganglions. In the medulla a few typical parenchymal and perivascular infiltrations were noted, but without definite cell necrosis. Lesions were not found elsewhere in the brain stem, in the olfactory bulbs, the lower thoracic sympathetics, the celiac and cervical spinal or lumbar spinal ganglions or in the spinal cord. Assuming that the few slight lesions in one lumbar sympathetic ganglion resulted from an inapparent infection from the earlier virus enema, Faber concludes that the lesions found in this monkey could all be explained on the assumption of a nerve borne infection entering through the oropharyngeal surfaces. He believes this entrance was "mainly through the fibers of the fifth, ninth and tenth nerves (probably including the gustatory) and to a lesser extent through the sympathetics." Thus the mouth and the pharynx appear to be more vulnerable to penetration by this virus than the lower portions of the alimentary tract.

TREND OF INFANT MORTALITY

No other country approaching the United States in race complexity and climatic diversity has as low a rate of infant mortality, according to a recent special report of the Bureau of the Census.[1] "In 1940," says this report, "the United States, with a rate of 47.0 per thousand live births, occupied the seventh position in the international rank order of infant death rates.

The lowest death rates were recorded for Norway, Sweden, Netherlands, Australia and New Zealand, the rates for these countries ranging between 37 and 39 infant deaths per thousand live births. Switzerland, with a rate of 46 per thousand live births in 1940, was the other country with a lower infant mortality rate than the United States.

The report also notes "that the 1940 infant death rate for Germany was 65 per thousand live births and for Italy 104, while the latest available rate (1936-1938) for Japan was 112 per thousand live births." Germany has had the most comprehensive system of compulsory sickness insurance for the longest period of any nation. The Nazis have succeeded in increasing the birth rate from 14.7 in 1933 to 20.4 in 1940, but the opinion is expressed that "this success was due to increased reemployment of the population and not to any elaborate 'population blueprints.'" This opinion seems to be confirmed by the increase in the United States from 16.6 in 1933 to 18.9 in 1941. The Monthly Vital Statistics Bulletin, Dec. 8, 1942, brings the information concerning the birth rate since that "for the first ten months of 1942 the provisional rate is 20.5 with indications that the rate is still rising."

1. Mortality Summary: The Infant, Nov. 30, 1942.

The most important period of infancy, from the standpoint of mortality, is at birth. In 1940, 13.9 per thousand infants born alive died during the first twenty-four hours after birth. . . . After the first day of life, the chances of survival of the newborn infant improve considerably. The death rate for the 1 day old infant is 3.5 per thousand live births, as compared with that of 13.9 per thousand live births for infants under 1 day of age.

However, when infant mortality statistics are correlated with the births attended by physicians and by midwives, holding total births constant, it is found that infant deaths are negatively associated with births attended by physicians and positively correlated with births attended by midwives. In each case the partial correlation coefficient is highly significant, but these coefficients cannot be interpreted to mean that there is a causal relationship between infant deaths and births attended by physicians or by midwives. The correlation coefficients merely indicate that there is a highly significant association existing between these factors and that infant mortality is lower in states with a large proportion of births attended by physicians and higher in states with a large proportion of births attended by midwives. Approximately the same degree of statistical association exists for infants of the white race but not for infants of other races.

DEMAND FOR FREE HEALTH SERVICE DECREASING

A comparison of the first quarter of 1941 with the same quarter in 1942 shows that there has been an increase in hospital inpatient care and a decrease in all other health programs, including clinic visits, home medical visits, medical social service, mental hygiene clinics, public health nursing and school health programs. The increase in hospital patient days is largely accounted for by increased service given in hospitals for tuberculosis. An analysis of the total inpatient days shows that there has been a decrease of 12.5 per cent in free patient days and an increase of 11.9 per cent in days paid for. This is primarily a reflection of improved economic conditions. When maternity care alone is considered there is a decrease of 6 per cent in those provided care under public auspices and an increase of 26 per cent in those paid for by the patients. The largest decrease (29 per cent) was in medical services provided by social agencies in the home and in doctors' visits to patients' homes reported by health and welfare agencies. These figures were obtained by a sampling test covering forty-five urban areas and other hospital statistics.[1]

THE JOURNAL OF THE NATIONAL MALARIA SOCIETY

The first volume of a new journal devoted to malaria has just appeared. It is the official organ of the National Malaria Society, formerly the National Malaria Committee. It is to be made a quarterly of fifty pages as soon as financial support and sufficient material justify such action. The first issue, which is the entire volume for 1942, contains some sixteen original contributions on various phases of the malaria problem. In view of the worldwide importance which is attached to control of malaria, this new journal will doubtless serve as a highly useful medium for disseminating information.

1. Social Statistics, November 1942, Supplement 1 to the Child, Vol. 7, U. S. Department of Labor, Children's Bureau, Washington, D. C.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS AND VETERINARIANS

PROCUREMENT OF MEDICAL OFFICERS FOR THE ARMY IN 1943

NOTE.—*The following is an official statement from the Medical Corps of the United States Army indicating the procedure to be followed in procuring medical officers for the Army during 1943.*—ED.

The Surgeon General is responsible for the procurement of medical officers for the Army of the United States. There is an Officer Procurement Service set up by the War Department for the procuring of applications of individuals for commission in the Army. The War Manpower Commission has set up a Procurement and Assignment Service for Physicians, Dentists and Veterinarians to designate the individuals who are essential to the community and those available for duty with the armed forces.

In order to coordinate the work of these two agencies, the Surgeon General has outlined the following procedure for the procurement of officers during the year 1943:

The state chairmen of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians will from time to time prepare lists of individuals who are declared available for duty. Their names will be sent to the Central Office of the War Manpower Commission in Washington, D. C. There a card will be prepared and sent to the individual informing him of the fact that he has been classified as available for military service and requesting that he send the attached card to the state chairman of the Procurement and Assignment Service signifying his interest in applying for a commission, and stating his preference for duty with the Army or Navy. Those who choose to serve in the Army may request that their papers be processed with the idea of assigning them to duty with the Air Forces.

The state chairmen will furnish the candidate to the designated field office of the Officer Procurement Service of the War Department. This office will request the individual physician, dentist or veterinarian to complete the proper application blanks and return them to that office and to have a final type physical examination, which will be accomplished at the nearest properly equipped army post.

The Officer Procurement District's office will forward the papers to the Surgeon General in Washington, who will then review the application for commission in the Medical Corps, Army of the United States. Those applications with the notation "Air" as designated will be referred to the Office of the Air Surgeon for further classification and assignment. Those applicants who are favorably considered will be notified at the earliest possible date by the Office of the Adjutant General that their recommendation is accepted and will receive orders to proceed to their proper station.

It is hoped by following this procedure that the Surgeon General will be able to provide an adequate medical service for our armed forces. It is contemplated that all individuals who are classified as essential to the civilian medical needs will not be asked to apply for a commission. No individual so classified need contact the Surgeon General or apply for a commission unless he can make arrangements with the state chairman of the Procurement and Assignment Service to have his classification changed from essential to available. The cooperation and interest of all physicians who are interested in military medical service will be appreciated, in that by proper application and processing of their case it will be much easier to provide necessary medical care for all parts of both the civilian and military services.

Concurrent with the changes in the military and civilian requirements for physicians and the changes in the recruiting procedures, the Surgeon General has announced the following policy, which will govern action to be taken in the consideration of ages and grades of initial appointments on all applicants effective Feb. 15, 1943:

1. Eligible applicants for appointment in the Medical Corps, Army of the United States, under the age of 38 will be appointed in the grade of first lieutenant only.

2. Eligible applicants between the ages of 38 and 55 will be appointed in the numbers and in the grade for which specific position vacancies exist.

There is an acute need for medical officers under 38 years of age. Applications are being solicited from physicians of this age group in those localities that have not furnished their quotas of physicians and where they are designed by the Procurement and Assignment Service as available for military service.

Appointments will be made by the Adjutant General of eligible applicants recommended by the Surgeon General and approved by the Secretary of War's Personnel Board.

NAVY

NAVAL MEDICAL SCHOOL GRADUATES

The following medical officers recently completed the basic course of instruction at the Naval Medical School, Bethesda, Maryland. Included also is each officer's home town and the hospital in which he served an internship. These medical officers were all lieutenants (j. g.) at the time of the completion of the course on November 28, except Ferdinand E. Chatard, Dana Alexander Weeks and Harold E. Williamson, who are lieutenants:

BARTON, HARRY LOUIS, Chicago, V(G), U. S. N. R., Ravenswood Hospital, Chicago, 1940-41.
BATEMAN, JAMES GORDON, Giffen, Mont., U. S. N., Highland-Alameda County Hospitals, Oakland, Calif., 1941-42.
BERESKY, TIBOR ANDREW, Chicago, U. S. N., Kings County Hospital, Brooklyn, 1941-42.
BERGMAN, GEORGE R., Los Angeles, U. S. N., U. S. Naval Hospital, San Diego, Calif., 1941-42.
BOND, THOMAS ARTHUR, Des Moines, Iowa, V(G), U. S. N. R., Ancker Hospital, St. Paul, 1937-38.
BRODY, SIDNEY IRVING, Philadelphia, U. S. N., Frankford Hospital, Philadelphia, 1941-42.
BROWN, LEO JEROME, Carbondale, Ill., V(G), U. S. N. R., City Hospital, St. Louis, 1937-38.
BROWN, MURRAY H., Rochester, Minn., U. S. N., Hartford Hospital, Hartford, Conn., 1938-40.
BURMAN, RICHARD GEORGE, Jeffersonville, Ind., V(G) U. S. N. R., Harper Hospital, Detroit, 1937-38.
CAMPBELL, JOHN ALLEN, Akron, Ohio, V(G), U. S. N. R., City Hospital of Akron, Ohio, 1941-42.
CHATARD, FERDINAND EDME, IV, Baltimore, U. S. N., Union Memorial Hospital, Baltimore, 1939-40.
CHRISTENSEN, ROLAND ARNOLD, Philadelphia (Yeadon), U. S. N., Wichita General Hospital, Wichita Falls, Texas, 1938-39.
DEYOE, GEORGE WILLIARD, New York, U. S. N., New York Medical College Hospital, New York, 1940-41.
DONELAN, EARL WILLIAM, Springfield, Ill., V(G), U. S. N. R., Cook County Hospital, Chicago, 1941-42.
DOWNS, ROGER SHERMAN, Litchfield, Conn., U. S. N., Strong Memorial Hospital, Rochester, N. Y., 1936-37.
DUFF, IVAN FRANCIS, Ann Arbor, Mich., V(G), U. S. N. R., University of Michigan Hospital, Ann Arbor, 1940-41.
DULLIGAN, PETER JAMES, JR., Brooklyn, U. S. N., St. Mary's Hospital, Brooklyn, 1941-42.
EMERSON, ROGER HILL, South Weymouth, Mass., V(G), U. S. N. R., Strong Memorial Hospital, Rochester, N. Y., 1941-42.
EPPLY, WALTER GEORGE, Manchester, N. H., V(G), U. S. N. R., Vancouver General Hospital, Vancouver, B. C., 1941-42.
FINCH, THOMAS VERNON, McComb, Miss., U. S. N., Philadelphia General Hospital, 1940-41.
FUNKE, ROBERT EDWARD, Long Beach, Calif., U. S. N., Los Angeles County General Hospital, 1941-42.
GAILLARD, RICHARD A., Yonkers, N. Y., U. S. N., Roosevelt Hospital, N. Y., 1941-42.
GALBALLY, JAMES FRANCIS, Germantown, Pa., U. S. N., Philadelphia General Hospital, 1941-42.
GASKILL, CORNELIA JANE, New York, W-V(S), U. S. N. R., Jersey City Medical Center, 1937-38.
GAUNT, JAMES JENNINGS, Milwaukee, V(G), U. S. N. R., Milwaukee County General Hospital, 1938-41.
GREENE, BIRAM MOE, Fremont, Ohio, U. S. N., U. S. Naval Hospital, Chelsea, Mass., 1941-42.
GREER, DURWARD, JR., Oakland, Calif., U. S. N., Highland-Alameda County Hospitals, Oakland, Calif., 1941-42.
HAYLES, ALVIN BEASLEY, Washington, D. C., U. S. N., U. S. Naval Hospital, Great Lakes, Ill., 1941-42.
HOPKINS, ARTHUR GEORGE, Brooklyn, U. S. N., Kings County Hospital, Brooklyn, 1941-42.
HOUSTON, WILLIAM BROCK, Akron, Ohio, V(G), U. S. N. R., City Hospital of Akron, Ohio, 1940-41.
JONES, EMORY ELLSWORTH, JR., Mount Hope, W. Va., V(G), U. S. N. R., Mercy Hospital, Baltimore, 1936-37.
MAGUIRE, FRANCIS HARBIN JAMES, San Diego, Calif., U. S. N., St. Agnes Hospital, Baltimore, 1937-38.
NOCKTON, RANSOM ANDREW, Crowley, La., V(G), U. S. N. R., Shreveport Charity Hospital, Shreveport, La., 1938-39.
PATTERSON, WALTER, Aldan, Pa., U. S. N., Hahnemann Hospital, Philadelphia, 1941-42.
PHYFE, HENRY PINKNEY, New York, V(G), U. S. N. R., Presbyterian Hospital, New York, 1941-42.
RAZZANO, CARMEN ITALO, Williston Park, N. Y., V(G), U. S. N. R., Knickerbocker Hospital, New York, 1937-40.
REYNOLDS, JOHN LUCIEN, Seattle, U. S. N., Stanford University Hospitals, San Francisco, 1940-41.
ROBERTSON, WILLIAM CRAIG, Atlanta, Ga., U. S. N., Employees Hospital, Tennessee Coal, Iron and Railroad Co., Fairfield, Ala., 1940-41.
ROBNETT, AUSEY H., Coronado, Calif., U. S. N., U. S. Naval Hospital, San Diego, Calif., 1941-42.
ROGERS, JOSEPH, Brooklyn, U. S. N., U. S. Naval Hospital, Brooklyn, 1941-42.
RUSSELL, GEORGE WASHINGTON, Little Rock, Ark., U. S. N., U. S. Naval Hospital, Bethesda, Md., 1941-42.
SCHROEDER, PAUL G., Wernersville, Pa., U. S. N., Reading Hospital, Reading, Pa., 1940-41.
SWINEY, MERRILL ALPHEUS, III, Bayonne, N. J. V(B), U. S. N. R., St. Mary's Hospital, Hoboken, N. J., 1941-42.
TEBOW, LOUIS ELLIOTT, Peoria, Ill., U. S. N., Norfolk Naval Hospital, Portsmouth, Va., 1941-42.
TRIMBUR, NEVIN RAY, Niles, Ohio, U. S. N., Youngstown Hospital Association, Youngstown, Ohio, 1939-41.
TURNER, ROBERT CORRELL, Mankato, Kan., V(G), U. S. N. R., University of Kansas Hospitals, Kansas City, Mo., 1941-42.
VAIL, GEORGE ALVIN, Fort Wayne, Ind., U. S. N., U. S. Naval Hospital, Great Lakes, Ill., 1941-42.
VEDDER, JAMES SHERMAN, Marshfield, Wis., V(G), U. S. N. R., Wesley Memorial Hospital, Chicago, 1937-38.
VENNER, ROBERT BROWNING, Hastings, Neb., U. S. N., Lenox Hill Hospital, New York, 1941-43.
WEEKS, DANA ALEXANDER, Peru, N. Y., V(S), U. S. N. R., Physicians Hospital of Plattsburgh, N. Y., 1935-36.
WILEY, JASON L., JR., Brooklyn, U. S. N., Kings County Hospital (Long Island Col. of Med. Div.), Brooklyn, 1941-42.
WILLIAMSON, HAROLD E., Arlington, Va., U. S. N., Memorial Hospital, Worcester, Mass., 1940-42.

CIVILIAN DEFENSE

THE EMERGENCY WATER SUPPLY PROGRAM

The Office of Civilian Defense, Washington, D. C., issued on December 22 Circular Medical Series No. 26, which contains the following recommendations for the guidance of state and local councils of defense in the emergency water supply program:

1. *Appointment and Duties of State Water Supply Coordinator.*—Responsibility for the organization and administration of the state emergency water supply program should be delegated to the state water supply coordinator, to be appointed as an official of the state defense council on recommendation of the state department of health. A member of the state agency having supervision over municipal water supplies would be a desirable appointee. He should be provided with technical and clerical assistants.

The state water supply coordinator should be responsible for the administration and organization of the state emergency water supply program and should represent the state in all matters pertaining to water supply as related to civilian defense. He should work in close cooperation with the state department of health or other state agency responsible for waterworks and with the regional sanitary engineers of the Office of Civilian Defense.

His duties should be to (1) prepare plans, rules and regulations for adoption by the state defense council and be responsible for administering the rules and regulations adopted; (2) institute and develop the mutual aid plan with the state, as suggested in U. S. Office of Civilian Defense Sanitary Engineering Bulletin No. 1, and be responsible for its operation at the state level during emergencies; (3) coordinate the emergency water supply program with other civilian defense activities at the state level; (4) develop a program for and coordinate the efforts of zone water supply coordinators, and (5) cooperate with the regional sanitary Engineer, U. S. Office of Civilian Defense, and develop interstate mutual aid.

2. *Appointment and Duties of Assistant State (Zone) Water Supply Coordinators.*—To facilitate execution of this program, zones or districts should be established with boundaries coterminous with other political or administrative divisions. Assistant state (zone) water supply coordinators should be appointed for these areas by the appointing authority on recommendation of the state water supply coordinator. Assistant state (zone) water supply coordinators should be selected from leading waterworks officials residing in the area. To assist this official, an engineer from one of the public health departments in the area may be appointed as deputy or assistant zone water supply coordinator. Individuals or small committees may also be designated by the zone water supply coordinator on a temporary basis to make special studies or investigations.

The duties of the assistant state (zone) water supply coordinator should be to (1) negotiate among the localities within the zone pacts for the operation and financing of the mutual aid plan and be responsible for the administration of the mutual aid program within the zone during emergencies; (2) establish and maintain contact with local councils of defense and integrate the local emergency water supply program within the state

program, and (3) advise local waterworks authorities on (*a*) technical aspects of emergency water works engineering, (*b*) recruitment and training of auxiliary personnel and emergency training of regular personnel, (*c*) procurement of materials and funds to execute plans and (*d*) integration of emergency water supply program with other local protective services.

3. In states where emergency water supply programs are being carried on by regular state departments as an adjunct to their regular duties, it is recommended that the program be officially recognized as a part of the civilian defense program of the state and its leaders be designated, as outlined in this letter.

4. In the administrative organization and operation of the emergency water supply program, it is most important that there be integration of the activities of local waterworks officials, state water supply coordinators and their assistant (zone) coordinators, and the regional sanitary engineers and the sanitary engineering section of the medical division of the U. S. Office of Civilian Defense.

WOMEN TO CARE FOR CHILDREN

The Office of Civilian Defense, Washington, D. C., announced on January 2 that civilian defense classes throughout the country have trained 38,676 women to care for war workers' children in day nurseries. These figures are based on reports from 745 local defense councils. Three hundred other councils have not yet reported.

MISCELLANEOUS

PUBLIC HEALTH UNDER HITLER

Nya Dagligt Kilahanda of Nov. 6, 1942 reports from Berlin that, as a result of a court verdict in the case of a man who had acted against his doctor's instructions and thus prolonged his illness, every German worker who falls ill and is unable to work is in duty bound to do everything possible to recover as soon as possible and avoid everything that is likely to make his condition worse or delay his recovery. He is absolutely bound to follow the doctor's instructions, and should he fail to do this or should he otherwise neglect his duty to recover he cannot count on receiving his wages during the time of his illness.

The *Völkischer Beobachter*, Vienna edition of Nov. 1, 1942, states that from the 250,000 applications with which the medical council is dealing at present it must be concluded that, apart from the several thousand patients who are in hospitals just now, there are 250,000 Viennese who are sick; this means that every seventh person is suffering from some ailment or other, apart from those weaklings who get contusions, sprains and broken ribs through riding in a tram between the Margaretenplatz and the Laudongasse. The diseases to which we are referring here are of a worse and more secretive character. No plaster casts, x-rays or medicine will help these patients. The only thing that could really save them from collapse is additional food, i. e., meat, rice, eggs, butter, fats, unskimmed milk and coffee. Because people lack this additional food, they feel sick and consult the doctor.

The *Brusseler Zeitung*, Oct. 17, 1942, reports that the German Academy in Brussels gives lectures for Belgium doctors, "thus enabling them to learn the German medical terminology and to hear about the development of hygiene in Germany."

According to *Minsker Zeitung* of Oct. 15, 1942, Dr. Wagner has published an article in the *Deutsches Arzteblatt* on the measures taken to prevent the spread of epidemics in the Ostland, which gives a complete survey of the conditions prevailing in the commissariats Ostland and Ukraine. It is said, *inter alia:*

"Statistics of the epidemics published by the Soviet authorities are false and are intended for propaganda purposes only. It can be assumed with certainty that on the average two or three million people succumbed annually to malaria in European Russia, of whom half were in the Ukraine, 200,000 to 500,000 to spotted typhus, particularly in White Ruthenia and in the northern Ukraine, and at least as many to typhus and dysentery.

"In 1942 every one had to report for medical examinations at first every four weeks, as from April last every week, and in the Ukraine every ten days. In addition measures were introduced in the Ostland to check the spread of lice among the population. A special scientific department was established in Riga for dealing with the spread of epidemics.

"Special importance was attached to the obtaining of vaccine lymph, medicaments, disinfectants, and so on. These had first to be imported from Germany; however, serum institutes had been established in Kaunas, Riga, Dorpat, Kiev and Dnepropetrovsk on the German model."

As stated in *Uj Magyarsag* of Oct. 14, 1942, a central x-ray institute has been founded in Kolozsvar (Cluj) and is now in operation. It contains wards with 15 beds and with 2 beds. It possesses radium to the value of 50,000 pengo and is primarily concerned with cancerous diseases.

According to the *Hamburger Fremdenblatt* of Oct. 30, 1942 the OKW has explained that also medical officers and personnel may win the sturmabzeichen if they operate under the same fighting conditions as the attacking infantry and care for the wounded in areas where there is close fighting. Similarly they may win the panzerkampfwagenabzeichen if they attend to the wounded during the fighting while riding in tanks.

Trots Allt of Oct. 8, 1942 states that the physiologist Richet has stated that the French food position is particularly dangerous for the young. Nine out of ten children are threatened with tuberculosis, and on the basis of the food rations nine tenths of the adults receive 1,030 calories instead of 3,000-4,000, which is necessary for working persons. Heavy workers receive 1,210 calories, which is less than the need for completely inactive men, i. e. 2,300 calories.

METHYL ALCOHOL UNDER COMPLETE ALLOCATION

Because of increased demands for military requirements, methyl alcohol, or methanol, was placed under complete allocation, effective January 15, with the issuance by the Director General for Operations of General Preference Order M-31 as amended. According to the Office of War Information, there will be an apparent shortage for 1943 of about 10 million gallons, excluding the methanol from wood distillation, unless the use of methanol for unessential items is curtailed as rapidly as possible. The increase in demand is caused primarily by the requirements for formaldehyde to produce hexamethylenetetramine, an ingredient in explosives used by both the United States and Great Britain. It also is caused by increasing demands for methanol to be used in the manufacture of methyl methacrylate resins for military aircraft and by increasing demands for hexamethylene tetramine for Russia.

BUTTER MAKERS TO RESERVE 30 PER CENT OF PRODUCTION

Manufacturers of creamery butter have been directed by Secretary of Agriculture Claude R. Wickard to set aside 30 per cent of their monthly production for direct war requirements beginning February 1. The order, Food Distribution Order No. 2, was issued to obtain sufficient supplies of butter to meet the needs of the armed forces and for minor export to Allied nations.

CLASSIFICATION OF COMMISSIONED OFFICERS, PUBLIC HEALTH SERVICE

The National Headquarters of the Selective Service System, Washington, D. C., issued Local Board Release No. 174 on December 26, which directed that registrants who are commissioned officers of the Public Health Service or Public Health Service Reserve, whether on active duty or in an inactive status, will be classified in class IV-B.

ORGANIZATION SECTION

THE PHYSICIAN'S FEDERAL INCOME TAX—1943

PREPARED BY THE BUREAU OF LEGAL MEDICINE AND LEGISLATION

The Revenue Act of 1942 has been correctly described as the greatest revenue raising measure in the history of our country and finds its justification in the tremendous needs of our war program, needs having to do with the actual expenditures for war purposes plus needs in relation to inflation potentialities. The act not only will spiral the tax burden of prior taxpayers but will bring into the income tax picture many millions of persons whose low income has heretofore constituted exempt income. Already plans are under way for additional legislation to raise still more revenue, and the tax burden may reasonably be expected to assume even greater proportions.

During the time when the new act was being formulated by congressional committees and when it was being discussed first in the House and in the Senate, advocates of the so-called Ruml pay-as-you-go plan for the payment of individual income taxes persistently suggested the undesirability of a continuation of the existing practice of taxing during a succeeding year the income received by an individual during a preceding year. There has recently been renewed interest in this plan, and the possibility is not remote that a changed policy may be adopted in the reasonably near future, perhaps by March 15. The President, the Treasury Department and leaders in the Congress have openly espoused the theory of the pay-as-you-go plan, and this espousal has given rise to some doubt on the part of taxpayers concerning the filing of returns this year. The doubt has been apparently so widespread as to call for a public statement by the chairman of the House Committee on Ways and Means, the committee that will initiate any change in our tax procedures, advising taxpayers that a return must be filed on or before March 15 and that that return must be based on the provisions of the 1942 Revenue Act. Despite the uncertainties of the future as to the pay-as-you-go matter, therefore, it is essential that the broad requirements of the new act be fully understood by federal income tax payers.

The Revenue Act of 1942 reduces the personal exemptions of single persons from $750 to $500 and of married persons or heads of families from $1,500 to $1,200. It reduces the credit for dependents from $400 to $350. An additional exemption is allowed members of the armed forces below the grade of commissioned officers. If a serviceman is single, then the first $250 of the service pay he received during 1942 is exempt. If he is married or the head of a family, then the first $300 is exempt. The determination of a taxpayer's status in the armed forces and his family status will be made as of the end of the taxable year for the purpose of this particular exemption.

The basic rate of taxation is increased from 4 per cent to 6 per cent. The surtax rate is elevated from 6 per cent on the first $2,000 of surtax net income to 13 per cent, with a constant increase in rates for incomes in the higher brackets. The earned income credit of 10 per cent remains as heretofore. This credit may be claimed in connection with the normal tax but not with the surtax.

The act continues the provision for a simplified tax schedule for use by taxpayers having gross incomes of $3,000 or less, derived wholly from salaries, wages or other forms of compensation for personal services, dividends, interest, rents, annuities or royalties. The use of the simplified form remains optional. If the taxpayer has no deductions, it will, generally speaking, be to his advantage to use this form. If he has deductions he should tentatively figure the tax under both the regular method and the optional method and use whichever method happens to be to his advantage.

Returns under the new act need not be made under oath, as has been the requirement heretofore. This will relieve taxpayers of the petty annoyance of having their returns sworn to before a notary public or some other official authorized to administer oaths. The taxpayer, however, who falsifies a return will be subject to heavy penalties even though he is not required to execute the return under oath.

WHO MUST FILE RETURNS

In General.—1. Returns must be filed by every unmarried person and by every married person not living with spouse, if gross income during 1942 was $500 or more.

2. Returns must be filed by every married person who lived with spouse, if gross income during 1942 was $1,200 or over. If both husband and wife had income and their combined gross income was $1,200 or over, they must either file separate returns or, if both are citizens or residents of the United States and if they were living together at the end of the taxable year, they may file a joint return. If a person was married and lived with spouse for only part of 1942, special rules apply with respect to the filing of returns, and physicians who come within this classification should read carefully the instructions given on the tax return blanks.

If the status of a taxpayer, so far as it affects the personal exemption or credit for dependents, changed during the year, the personal exemption and credit must be apportioned, under rules and regulations prescribed by the Commissioner of Internal Revenue with the approval of the Secretary of the Treasury, in accordance with the number of months before and after such change. For the purpose of such apportionment a fractional part of a month should be disregarded unless it amounts to more than half a month, in which case it is to be considered as a month.

Physicians in Military or Naval Service.—The fact that a physician may be in service does not of itself excuse a failure to file a return, for the income tax act applies to persons in service as well as to persons engaged in civilian activities. Physicians who have

gone into service, therefore, should if at all possible file complete returns before the deadline. While, unfortunately, definite regulations have not been issued to cover the situation, it is understood that, if because of the inaccessibility of necessary records a physician in service is unable to file a complete return, he may file a tentative return on which he must estimate his income, deductions and tax as best he can and indicate on the return his reasons for following this procedure. He will be required at a later date to file a complete return, and necessary adjustments in the tax will be made.

If a physician in service is on duty outside the United States no income tax return or payment of any income tax will become due, generally speaking, until the fifteenth day of the third month following the month in which the physician ceases (except by reason of death or incompetency) to be a member of the military forces on sea duty or in service outside the continental United States, or the fifteenth day of the third month following the month in which the present war is terminated as proclaimed by the President, whichever may be the earlier.

GROSS AND NET INCOMES: WHAT THEY ARE

Gross Income.—A physician's gross income is the total amount of money received by him during the year for professional services, regardless of the time when the services were rendered for which the money was paid, assuming that the return is made on a cash receipts and disbursements basis, plus such money as he has received as profits from investments and speculation and as compensation and profits from other sources.

If a physician receives a salary as compensation for services rendered and in addition thereto living quarters or meals, the value to the physician of the quarters and meals so furnished ordinarily constitutes income subject to tax. If, however, living quarters or meals are furnished for the convenience of the employer, the value thereof need not be computed and added to the compensation otherwise received by the physician. As a general rule, the test of "convenience of the employer" is satisfied if living quarters or meals are furnished to a physician who is required to accept such quarters and meals in order to perform properly his duties. For example, if a physician employed by a hospital is subject to immediate service at any time during the twenty-four hours of the day and therefore cannot obtain quarters or meals elsewhere without material interference with his duties and on that account is required by the hospital to accept the quarters or meals furnished by it, the value thereof need not be included in the gross income of the physician.

Net Income.—Certain professional expenses and the expenses of carrying on any enterprise in which the physician may be engaged for gain may be subtracted as "deductions" from the gross income, to determine the net income on which the tax is to be paid. An "exemption" is allowed, the amount depending on the taxpayer's marital status during the tax year as stated before. These matters are fully covered in the instructions on the tax return blanks.

Earned Income.—In computing the normal tax, but not the surtax, there may be subtracted from net income from all sources an amount equal to 10 per cent of the earned net income, except that the amount so subtracted shall in no case exceed 10 per cent of the net income from all sources. Earned income means professional fees, salaries and wages received as compensation for personal services, as distinguished from receipts from other sources.

The first $3,000 of a physician's net income from all sources may be regarded under the law as earned net income, whether it was or was not in fact earned within the meaning set forth in the preceding paragraph. Net income in excess of $3,000 may not be claimed as earned unless it in fact comes within that category. No physician may claim as earned net income any income in excess of $14,000.

PHYSICIANS IN MILITARY OR NAVAL SERVICE

As previously pointed out, physicians in service are as much subject to the income tax law as are physicians engaged in civilian practice. The service pay of such physicians must be reported as income. Commutation of quarters and rental value of quarters occupied by medical officers, however, are not taxable income.

If the ability of physicians in service to pay income taxes is materially affected by such service, payment of the tax falling due before or during the service may be deferred for a period extending not more than six months after termination of service. This deferment is authorized by section 513 of the Soldiers' and Sailors' Civil Relief Act of 1940 and applies to all members of the Army, Navy, Marine Corps and Coast Guard, and to all officers of the United States Public Health Service detailed by proper authority for duty either with the Army or Navy, on active duty or undergoing training or education under the supervision of the United States preliminary to induction into service. This does not apply to the tax imposed on employers by section 1400 of the Federal Insurance Contributions Act. This deferment is not automatic. The taxpayer must present evidence to show that his ability to pay the tax is materially impaired by reason of military service. Proof of that impairment should be submitted at the time the tax is due, on a form procurable from the offices of the collectors of internal revenue. A copy of the form was reproduced in the Feb. 28, 1942 issue of THE JOURNAL on page 737.

THE VICTORY TAX

The physician need give no consideration to the new 5 per cent Victory tax in making his return on or before March 15. As explained in THE JOURNAL, Dec. 5, 1942, this tax does not apply to income received during 1942, although physicians who are classifiable as employees will periodically have the tax withheld from their salaries during 1943.

TAXATION OF ACCOUNTS RECEIVABLE

The Revenue Act of 1942 remedies an unjust method of taxation that has heretofore prevailed in connection with the unpaid accounts on the books of a taxpayer at the time of his death. Under prior law, for the year of death, the value of such accounts has been included as income and subject to the income tax rates, even though the taxpayer actually received no income at all therefrom. Hereafter the value of the unpaid accounts will not be considered as a part of the income of the decedent for the year of death but will be taxable when paid, as a part of the income of the person receiving the money. A detailed discussion of this matter was published in THE JOURNAL, Jan. 10, 1942, page 149.

DEDUCTIONS FOR PROFESSIONAL EXPENSES

A physician is entitled to deduct all current expenses necessary in carrying on his practice. The taxpayer should make no claim for the deduction of expenses unless he is prepared to prove the expenditure by competent evidence. So far as practicable, accurate itemized records should be kept of expenses and substantiating evidence should be carefully preserved. The following statement shows what such deductible expenses are and how they are to be computed:

Office Rent.—Office rent is deductible. If a physician rents an office for professional purposes alone, the entire rent may be deducted. If he rents a building or apartment for use as a residence as well as for office purposes, he may deduct a part of the rental fairly proportionate to the amount of space used for professional purposes. If the physician occasionally sees a patient in such dwelling house or apartment, he may not, however, deduct any part of the rent of such house or apartment as professional expense; to entitle him to such a deduction he must have an office there, with regular office hours. If a physician owns the building in which his office is located, he cannot charge himself with "rent" and deduct the amount so charged.

Office Maintenance.—Expenditures for office maintenance, as for heating, lighting, telephone service and the services of attendants are deductible.

Supplies.—Payment for supplies for professional use are deductible. Supplies may be fairly described as articles consumed in the using; for instance, dressings, clinical thermometers, drugs and chemicals. Professional journals may be classified as supplies and the subscription price deducted. Amounts currently expended for books, furniture and professional instruments and equipment, "the useful life of which is short," generally less than one year, may be deducted; but if such articles have a more or less permanent value, their purchase price is a capital expenditure and is not deductible.

Equipment.—Equipment comprises property of a more or less permanent nature. It may ultimately wear out, deteriorate or become obsolete, but it is not in the ordinary sense of the word "consumed in the using."

The cost of equipment such as has been described, for professional use, cannot be deducted as expense in the year acquired. Examples of this class of property are automobiles, office furniture, medical, surgical and laboratory equipment of more or less permanent nature, and instruments and appliances constituting a part of the physician's professional outfit, to be used over a considerable period of time, generally over one year. Books of more or less permanent nature are regarded as equipment and the purchase price is therefore not deductible.

Although the cost of such equipment is not deductible in the year acquired, nevertheless it may be recovered through depreciation deductions taken year by year over its useful life, as described later.

No hard and fast rule can be laid down as to what part of the cost of equipment is deductible each year as depreciation. The amount depends to some extent on the nature of the property and on the extent and character of its use. The length of its useful life should be the primary consideration. The most that can be done is to suggest certain average or normal rates of depreciation for each of several classes of articles and to leave to the taxpayer the modification of the suggested rates as the circumstances of his particular case may dictate. As fair, normal or average rates of depreciation, the following have been suggested: automobiles, 25 per cent a year; ordinary medical libraries, x-ray equipment, physical therapy equipment, electrical sterilizers, surgical instruments and diagnostic apparatus, 10 per cent a year; office furniture, 5 per cent a year.

The principle governing the determination of all rates of depreciation is that the total amount claimed by the taxpayer as depreciation during the life of the article, plus the salvage value of the article at the end of its useful life, shall not be greater than its purchase price or, if purchased before March 1913, either its fair market value as of that date or its original cost, whichever may be greater. The physician must in good faith use his best judgment and claim only such allowance for depreciation as the facts justify. The estimate of useful life, on which the rate of depreciation is based, should be carefully considered in his individual case.

Medical Dues.—Dues paid to societies of a strictly professional character are deductible. Dues paid to social organizations, even though their membership is limited to physicians, are personal expenses and not deductible.

Postgraduate Study.—The Commissioner of Internal Revenue holds that the expense of postgraduate study is not deductible.

Traveling Expenses.—Traveling expenses, including amounts paid for transportation, meals and lodging, necessarily incurred in professional visits to patients and in attending medical meetings for a professional purpose, are deductible.

Automobiles.—Payment for an automobile is a payment for permanent equipment and is not deductible. The cost of operation and repair, and loss through depreciation, are deductible. The cost of operation and repair includes the cost of gasoline, oil, tires, insurance, repairs, garage rental (when the garage is not owned by the physician), chauffeurs' wages, and the like.

Deductible loss through depreciation of an automobile is the actual diminution in value resulting from obsolescence and use and from accidental injury against which the physician is not insured. If depreciation is computed on the basis of the average loss during a series of years, the series must extend over the entire estimated life of the car, not merely over the period in which the car is possessed by the present taxpayer.

If an automobile is used for professional and also for personal purposes—as when used by the physician partly for recreation, or so used by his family—only so much of the expense as arises out of the use for professional purposes may be deducted. A physician doing an exclusive office practice and using his car merely to go to and from his office cannot deduct depreciation or operating expenses; he is regarded as using his car for his personal convenience and not as a means of gaining a livelihood. What has been said in respect to automobiles applies with equal force to horses and vehicles and the equipment incident to their use.

MISCELLANEOUS

Contributions to Charitable Organizations.—For detailed information with respect to the deductibility of charitable contributions generally, physicians should

consult the official return blank or obtain information from the collectors of internal revenue or from other reliable sources. A physician may not, however, deduct as a charitable contribution the value of services rendered an organization operated for charitable purposes.

Bad Debts.—Physicians who make their returns on a cash receipts and disbursements basis, as most physicians do, cannot claim deductions for bad debts.

Taxes.—Taxes generally, either federal or state, are deductible by the person on whom they are imposed by law. Both real and personal property taxes are deductible; but so-called taxes, more properly assessments, paid for local benefits, such as street, sidewalk, and other like improvements, imposed because of and measured by some benefit inuring directly to the property against which the assessment is levied, do not constitute an allowable deduction from gross income. Physicians may deduct state gasoline taxes and state sales taxes. In some states sales taxes are imposed on the seller, but, if they are passed on to the buyer, the latter may deduct them.

State income and use taxes are deductible; federal income taxes are not. Among the federal taxes that a physician may deduct are those on admissions, dues, initiation fees, safety deposit boxes, tax on telegraph, telephone, cable and radio messages, and the federal use tax on automobiles. State automobile license fees are deductible. If a state or local fee is imposed for regulatory purposes, and not to raise revenue, the fee may not ordinarily be deducted as a tax. If such fees, however, are classifiable as a business expense, they are deductible as such. Annual registration fees imposed on physicians probably come within the category of regulatory fees and should be deducted as a business expense rather than as taxes. Local and state occupational taxes imposed on physicians are deductible either as taxes or as a business expense, depending on the purpose for which the tax is imposed.

The excise taxes imposed on employers by section 804, title VIII, and section 901, title IX, of the Social Security Act, commonly referred to as old age and unemployment benefit taxes, are deductible annually by employers in computing net income for federal income tax purposes. If the taxpayer's return is made on a cash basis, as are the returns of practically all physicians, the taxes are deductible for the year in which they are actually paid. If the return is made on an accrual basis, the taxes are deductible for the year in which they accrue, irrespective of when they are actually paid. Employees, including physicians whose employment brings them within that category, may not deduct the tax imposed on them by section 801, title VIII, of the Social Security Act, generally referred to as the old age benefits tax. If, however, the employer assumes payment of the employee's tax and does not withhold the amount of the tax from the employee's wages, the amount of the tax so assumed may be deducted by the employer, not as a tax paid but as an ordinary business expense.

Medical Expense.—A taxpayer may deduct amounts expended for medical, dental and hospital care, not compensated for by insurance or otherwise, including amounts paid for accident and health insurance, according to a prescribed formula. Deductions will be permitted to the extent that such expenses exceed 5 per cent of the net income of the taxpayer but not in excess of $2,500 in case of the head of a family, or $1,250 in case of other individual taxpayers.

Equipment Necessitated by Military Service.—The cost of equipment of an Army officer to the extent only that it is especially required for his profession and does not merely take the place of articles required in civilian life is deductible. The cost of a uniform is considered a personal expense and hence not deductible.

Laboratory Expenses.—The deductibility of the expenses of establishing and maintaining laboratories is determined by the same principles that determine the deductibility of corresponding professional expenses. Laboratory rental and the expenses of laboratory equipment and supplies and of laboratory assistants are deductible when under corresponding circumstances they would be deductible if they related to a physician's office.

Losses by Fire or Other Causes.—Loss of and damage to a physician's equipment by fire, theft or other cause, not compensated by insurance or otherwise recoverable, may be computed as a business expense and is deductible, provided evidence of such loss or damage can be produced. Such loss or damage is deductible, however, only to the extent to which it has not been made good by repair and the cost of repair claimed as a deduction.

Insurance Premiums.—Premiums paid for insurance against professional losses are deductible. This includes insurance against damages for alleged malpractice, against liability for injuries by a physician's automobile while in use for professional purposes, and against loss from theft of professional equipment and damage to or loss of professional equipment by fire or otherwise. Under professional equipment is to be included any automobile belonging to the physician and used for strictly professional purposes.

Expense in Defending Malpractice Suits.—Expense incurred in the defense of a suit for malpractice is deductible as a business expense.

Sale of Spectacles.—Oculists who furnish spectacles etc., may charge as income money received from such sales and deduct as an expense the cost of the article sold. Entries on the physician's account books should in such cases show charges for services separate and apart from charges for spectacles, etc.

NONTRADE OR NONBUSINESS EXPENSES

A new provision in the Revenue Act of 1942 permits, in the case of an individual, the deduction of all the ordinary, necessary expenses paid or incurred during the taxable year for the production or collection of income, or for the management, conservation or maintenance of property held for the production of income. While the phraseology of this provision is very broad, the Commissioner of Internal Revenue has by regulation ruled that the following expenses, among others, are not deductible under it: Commuters' expenses; expenses of taking special courses of training; expenses in seeking employment or in placing one's self in a position to begin rendering personal services for compensation; bar examination fees and other expenses incurred in securing admission to the bar, and corresponding fees and expenses incurred by physicians, dentists, accountants and other taxpayers for securing the right to practice their respective professions.

OFFICIAL NOTES

DOCTORS AT WAR

Radio broadcasts of Doctors at War by the American Medical Association in cooperation with the National Broadcasting Company and the medical department of the United States Army and the United States Navy are on the air each Saturday at 5 p. m. Eastern War Time (4 p. m. Central War Time, 3 p. m. Mountain War Time, 2 p. m. Pacific War Time). An exception is the Chicago area, where the broadcasts are heard by transcription at 8 p. m. Central War Time Saturdays on station WMAQ.

Titles, subjects and guest speakers where scheduled for the next five programs are as follows:

January 30. Wake Up America: social hygiene and the war. Guest speaker Surg. Gen. Thomas Parran, United States Public Health Service.

February 6. Rumor Monger: morale in wartime.

February 13. The Heart of a Soldier: strong hearts in the Army.

February 20. "Come and Get It"—the story of how our fighting men are fed.

February 27. "Community Fortress"—health on the home front.

HOMEMAKERS' PROGRAM ON WLS

Beginning January 28 and each Thursday thereafter to and including May 27, the American Medical Association will broadcast during the Homemakers' Hour on radio station WLS, Chicago, a program intended to be helpful to the mothers of young children, under the title "Before the Doctor Comes." Common home health problems will be discussed in an interview program in which Dr. W. W. Bauer, Director of the Bureau of Health Education, will be interviewed by Mrs. Harriet H. Hester. The program will be heard on radio station WLS (890 kilocycles) between 1:30 and 2 p. m. as a part of the Homemakers' Hour. Following are the topics for the first three broadcasts:

January 28. The Child with Sniffles.
February 4. The Child with a Sore Throat.
February 11. The Child with a Cough.

This is not a network program, but station WLS is a 50,000 watt, clear channel station which has a primary daytime coverage of the states of Wisconsin, Michigan, Indiana and Illinois with portions of Iowa, Missouri, Ohio and occasionally Kentucky. The audience is 60 to 70 per cent "down state."

MEDICAL LEGISLATION

DISTRICT OF COLUMBIA

Bills Introduced.—S. 242, introduced by Senator Capper, Kansas, provides for the issuance of a license to practice osteopathy in the District of Columbia to Maria G. Waksmundzka. H. R. 741, introduced by Representative Randolph, West Virginia, provides for the registration of births in the District of Columbia that were not registered when the births occurred in the District.

MEDICAL BILLS IN CONGRESS

Bills Introduced.—S. J. Res. 12, introduced by Senator Wheeler, Montana, proposes to amend an act passed by the Seventy-Seventh Congress to regulate the interstate sale of dentures by postponing the effective date of that act for a period of six months. S. 72, introduced by Senator McNary, Oregon, proposes service pensions to all persons who served ninety days in foreign service under the jurisdiction of the Quartermaster General, Surgeon General of the United States Army, the Secretary of the Navy or the Marine Corps during the Spanish-American War, including the Philippine Insurrection and the Chinese Boxer Rebellion. S. 77, introduced by Senator Caraway, Arkansas, proposes to authorize the Secretary of the Treasury to determine the total amount collected by the federal government from each physician during the period June 1, 1920 to June 30, 1931 for the privilege of prescribing the hot waters from the Hot Springs National Park and to refund to each such physician the total amount so determined to have been collected from him, with the proviso that not more than $660 may be returned to any one physician. S. 137, introduced by Senator Davis, Pennsylvania, provides that no person shall be discriminated against, in the administration of the civil service laws and regulations, in any case because of his or her blindness or impaired visual acuity. S. 180, introduced by Senator LaFollette, Wisconsin, provides for the vocational rehabilitation, education, training and the rendition of other services to persons disabled while members of the armed forces or disabled in war industries or otherwise. S. 186, introduced by Senator White for himself and Senator Brewster, both of Maine, proposes to create a Division of Water Pollution Control in the United States Public Health Service. S. 187, introduced by Senator Walsh, Massachusetts, provides for vocational rehabilitation and the return to civil employment of certain persons disabled under circumstances entitling them after discharge or separation from the military or naval forces of the United States to a pension or retirement pay. S. 216, introduced by Senator Reynolds, North Carolina, proposes to amend certain provisions of the National Defense Act of June 3, 1916 by eliminating the Medical Administrative Corps in the Medical Department of the regular Army and substituting therefor a Pharmacy Corps. S. 230, introduced by Senator Clark, Missouri, proposes to amend existing veterans' regulations so as to grant hospitalization, domiciliary care and burial benefits to any officer, enlisted man, member of the Army Nurse Corps (female) or Navy Nurse Corps (female) employed in the active military or naval service of the United States on or after Dec. 7, 1941 and before the termination of the present war. S. 281, introduced by Senator Green, Rhode Island, proposes to amend and extend the provisions of the Social Security Act, to extend the coverage of federal old age and survivors insurance, to provide insurance benefits for workers permanently and totally disabled, to provide hospitalization benefits, to provide special federal aid to states for public assistance, to provide federal grants to states for general public assistance and to amend the provision for federal grants to states for old age assistance, aid to dependent children and aid to the blind. H. R. 121, introduced by Representative Cannon, Missouri, provides that all public laws granting medical and hospital treatment, domiciliary care, compensation and other allowances, pensions, disability allowance and retirement pay to veterans and the dependents of veterans of the World War which were repealed in 1933 shall be reenacted. H. R. 375, introduced by Representative Voorhis, California, proposes to amend the Social Security Act so as to provide that each state shall have the exclusive right to adopt its own interpretation of the phrases "needy individuals who are blind" and "blind individuals who are needy." The purpose of the bill is to encourage the states to make more adequate provisions for blind persons. H. R. 376, introduced by Representative Voorhis, California, undertakes to amend the Social Security Act so that each state may have the exclusive right to adopt its own interpretation of the phrases "needy individuals" as used in the act. The purpose of this bill is to encourage the states to make more adequate provisions for aged persons. H. R. 661, introduced by Representative Rogers, Massachusetts, proposes, for the purpose of enabling the Public Health Service to assist states, counties, cities or other political subdivisions of the states to extend and improve measures through public and private institutions and organizations for the diagnosis, treatment and control of cancer, including the provision of hospital, diagnostic, clinic and other facilities for the diagnosis and treatment of persons suffering from cancer or suspected of suffering from this disease, that there be appropriated for the first fiscal year of the operation of the law the sum of $2,300,000 and for each fiscal year thereafter such sum as may be necessary to carry out its purposes. H. R. 723, introduced by Representative Green, Florida, proposes to authorize an appropriation of $1,550,000 for the con-

struction of a marine hospital in the state of Florida, the site to be selected by the Federal Board of Hospitalization. H. R. 724, introduced by Representative Green, Florida, proposes an appropriation of $2,500,000 for the construction of a marine hospital at Jacksonville, Fla. H. R. 728, introduced by Representative Green, Florida, proposes to authorize the Administrator of Veterans' Affairs, within the limits of Veterans' Administration facilities, to furnish necessary dental care and treatment, including necessary dental appliances and transportation to and from a Veterans' Administration facility, to veterans of any war (including the Indian wars, the Boxer Rebellion and the Philippine Insurrection) who were not dishonorably discharged and are not entitled to the benefits provided by the bill under any law or veterans regulation in effect at the present time. H. R. 735, introduced by Representative Welch, California, proposes that all persons who served in a civilian capacity under the jurisdiction of the Quartermaster General during the war with Spain, the Philippine Insurrection or the China Relief Expedition on vessels owned by the United States and engaged in the transportation of troops, supplies, ammunition or materials of war, and who were discharged for disability incurred in such governmental service in line of duty, shall be furnished medical and hospital treatment and domiciliary care in Veterans' Administration facilities in the same manner and to the same extent as provided for veterans of any war. H. R. 739, introduced by Representative Van Zandt, Pennsylvania, and H. R. 801, introduced by Representative Rankin, Mississippi, provide for the rehabilitation of disabled veterans of the present war. H. R. 782, introduced by Representative Voorhis, California, proposes to direct the Administrator of Veterans' Affairs to promulgate regulations pertaining to service connection, containing additional provisions requiring that, as to those veterans who are shown to have been engaged in combat with an enemy of the United States or who are shown to have been subjected to other arduous conditions of military or naval service, any subsequent disability which could have resulted by way of incurrence or aggravation traceable to such veteran's active military or naval service shall be considered as directly due to or aggravated by such service in line of duty. H. R. 783, introduced by Representative Voorhis, California, proposes to grant permanent and total disability ratings to veterans suffering from severe industrial inadaptability as a result of war service. H. R. 786, introduced by Representative Tolan, California, proposes to amend section 40 of the United States Employees' Compensation Act so as to authorize chiropractors to treat beneficiaries of that act. H. R. 788, introduced by Representative Tolan, California, proposes to amend the Social Security Act so as to provide grants to states for needy disabled adults. H. R. 789, introduced by Representative Tolan, California, proposes to provide grants to the states for assistance in the rehabilitation of disabled persons incapacitated for normal employment. H. R. 790, introduced by Representative Rankin, Mississippi, provides that all compensation, pension and hospital privileges granted to veterans of the first world war, their widows and dependents shall be extended to veterans of the present war, their widows and dependents. H. R. 828, introduced by Representative Costello, California, proposes to authorize an appropriation of $2,600,000 for the construction of a marine hospital in or near Los Angeles. H. R. 867, introduced by Representative Knutson, Minnesota, proposes to exempt from the operations of the Social Security Act associations furnishing medical care or hospitalization to members or their dependents if no part of the net earnings of the association inures to the benefit of any private shareholder or individual and if 75 per cent or more of the income consists of amounts collected from members or contributed by the employer for the sole purpose of making such payments and meeting expenses. H. R. 868, introduced by Representative Knutson, Minnesota, proposes to amend the Social Security Act by providing for grants to states for furnishing aid to needy individuals who are physically handicapped. H. R. 874, introduced by Representative Knutson, Minnesota, undertakes to amend the Selective Training and Service Act of 1940 by providing that each member of each local board shall receive as compensation for his services $5 for each day on which he performs board duties and in addition shall receive travel expenses at the rate of 5 cents per mile and subsistence expenses while away from his official station on duties of the board. H. R. 887, introduced by Representative Van Zandt, Pennsylvania, provides that any person who served in the military or naval forces of the United States during a recognized campaign or expedition and who was honorably separated from such service shall be granted hospitalization and domiciliary care by the Veterans' Administration subject to the same restrictions and limitations as are applicable to World War veterans. H. R. 889, introduced by Representative Van Zandt, Pennsylvania, proposes to provide total disability ratings for veterans with severe functional nervous diseases or psychoneurotic conditions. H. R. 891, introduced by Representative Voorhis, California, provides for the granting of permanent and total disability ratings to veterans suffering from severe industrial inadaptability as a result of war service. H. R. 899, introduced by Representative Kennedy, New York, provides compensation for injuries or death sustained by volunteer civilian defense workers in line of duty. The bill also provides that for any injury sustained by an air raid warden or other volunteer worker engaged in civilian defense while in the performance of duty, whether or not disability has arisen, the United States shall furnish to the injured person all services, appliances and supplies prescribed or recommended by duly qualified physicians which, in the opinion of the United States Employees' Compensation Commission, are likely to cure or relieve or to reduce the degree or the period of disability or to aid in lessening the amount of the monthly compensation. H. R. 911, introduced by Representative Rees, Kansas, provides that any veteran entitled to civil service preference shall have the right to be examined and to qualify for appointment to any position under classified civil service, notwithstanding his need of a prosthetic appliance to overcome a handicap, if the duties of the position for which qualification is sought can be performed by such veteran. H. R. 913, introduced by Representative Rankin, Mississippi, proposes to extend the privilege of hospitalization to veterans of World War II for the treatment of non-service connected disabilities and to provide for preference of hospitalization to those veterans who were discharged by reason of disability and to those entitled to benefits for service connected disabilities.

STATE MEDICAL LEGISLATION

Arizona

Bills Introduced.—S. 9 proposes the enactment of a premarital examination law. The certificate to be obtained by each applicant for a marriage license must be executed by a licensed physician and shall certify that the applicant has been given an examination and been found not to be infected with syphilis in a communicable stage. The standard serologic test required shall be made at a laboratory either within or without the state which has been approved by the state board of health and the physician's fees and charges for making the examination and issuing the certificate required shall not exceed $3 for each person examined. S. 13 proposes the enactment of an occupational disease act. Occupational disease is defined to mean a disease which is due to causes and conditions characteristic of and peculiar to a particular trade, occupation, process or employment and excludes all ordinary diseases of life to which the general public is exposed. Among other things, the bill proposes that in the event an employee, though not actually incapacitated, is found to be affected by silicosis or asbestosis, he may, subject to the approval of the commission, waive in writing full compensation for any aggravation of condition that may result from continuing in the hazardous occupation. In case of total incapacity or death as a result of the disease, after waiver, however, compensation not to exceed $3,000, whether for incapacity, death or both, shall nevertheless be payable. The proposed bill further provides for the appointment of an advisory medical council of three members who shall be licensed practitioners of medicine in good professional standing and qualified in the diagnosis and treatment of occupational diseases, at least one of whom shall be an experienced roentgenologist. The council shall conduct examinations, make reports on controverted medical questions and assist in any postmorten examination directed by the commission, and the report of such advisory medical council shall become part of the record of the case and be accepted and considered by the commission as expert medical testimony, unless a special hearing is requested by the claimant

for the purpose of examining or cross examining members of the council. S. 23 proposes to empower the state department of health to commit any person known to be infected with a venereal disease to an institution for care and treatment and to detain and quarantine such person for such time as may be necessary. The proposal would further provide that a person wilfully refusing to submit to treatment by the state board of health would be guilty of a misdemeanor.

Arkansas

Bill Introduced.—S. 13 proposes to amend the medical practice act by repealing Act No. 368 of the Laws of 1941, which required an annual license and registration of licentiates and amended certain provisions regarding educational requirements and the granting of reciprocity certificates.

California

Bills Introduced.—S. 81 and A. 186 propose to amend the sales tax by exempting therefrom the sale of medicines sold as dietary supplements or adjuncts. A. 6 proposes to amend the osteopathic practice act by eliminating the existing requirement that osteopaths, at the time of the annual renewal of their licenses, present satisfactory evidence of the completion, during the preceding year, of a minimum of thirty hours of professional educational work as approved by the ostheopathic board. A. 44 proposes to amend the Revenue and Taxation Code by exempting from the sales tax medicines or drugs, defined to include any substance or mixture of substances intended to be used internally or externally in the diagnosis, cure, treatment or prevention of diseases of man. A. 80 proposes to amend the Revenue and Taxation Code so as to include the sales of medicines used as dietary supplements or adjuncts. A. 129 proposes to amend the Revenue and Taxation Code by exempting from the sales tax the sale of medicines and drugs used in the diagnosis, cure, mitigation, treatment or prevention of disease in man, but not including any instrument or apparatus. A. 152 proposes the appropriation of $2,000,000 to the regents of the University of California to be expended for the erection and equipment of a hospital to be maintained and supported by the regents in conjunction with the medical school of the University of California. A. 227 proposes to amend the law relative to the liability of innkeepers so as to include hospitals by providing that a hospital shall be liable for losses of or injuries to personal property belonging to patients to the same degree as would a depositary for hire and providing further that if the hospital keeps a fireproof safe and notifies the patient to that effect then it is not liable for loss or damage to the personal property of a patient except so far as the acts of the hospital contribute thereto. A. 230 proposes to authorize payments, out of the general funds of a city, city and county, or county, of a physician's fee for issuing a food certificate to any person needing more than the ration thereof might provide. A. 292 proposes to amend the state labor code by prohibiting an employer or insurance company writing compensation insurance from contracting with any physician, hospital or other person for the medical or surgical care or hospitalization of any injured person on the basis of such physician, hospital or other person receiving a percentage of the gross premiums collected by such insurance company or on the basis of any percentage of such employer's payroll or on the basis of any fixed charges which are less than the reasonable value of such services as fixed by rates adopted by the industrial accident commission. The bill would further prohibit a physician, hospital or other person from paying over to an employer or insurance carrier any rebate for sums received for the medical or surgical care or hospitalization of any injured employee. A. 326 proposes to amend the Business and Professions Code relating to the practice of nursing by exempting therefrom the performance of certain services in case of an individual emergency and during a national emergency arising out of war or during an epidemic or other public disaster. A. 327 proposes to amend the health and safety code regulating the licensing of clinics, dispensaries and maternity hospitals by exempting from such regulation a hospital corporation organized and operated exclusively for charitable purposes. A. 328 proposes an amendment to the civil code which would create a lien in favor of doctors and hospitals for reasonable charges for hospital care, treatment and maintenance of an injured person, including drugs, supplies and x-ray and laboratory services, on any recovery of any sum had or collected by such injured person whether by judgment or by settlement, not to exceed, however, 50 per cent of such recovery. The proposal then sets forth certain notice requirements which the hospital or physician must give and provides a penalty against any person making payment or settlement of a claim without paying the amount covered by the lien. These provisions would not be applicable to claims arising under the workmen's compensation act, claims for wrongful death or negligent injury to a minor or claims for wrongful death to an adult or minor leaving a husband, wife or children. A. 329 proposes to amend the law relating to medical and hospital care to indigents by prohibiting the board of supervisors from letting the care, maintenance or attendance of such indigent sick or dependent poor by contract to any person, except that in cases of unusual difficulty or which require treatment or the use of facilities not immediately available in the county and in cases of emergency the board may secure by contract hospital care within or without the county, including medical, surgical, x-ray, laboratory, nursing and general hospital service at a cost not exceeding the fair and reasonable value thereof, in either a private or a state supported institution. A. 334 proposes to amend the Business and Professions Code relating to the practice of chiropody by redefining chiropody to mean the diagnosis, medical, surgical, mechanical, manipulative and electrical treatment of the human foot and leg. The "and leg" is new and is substituted for the words "including the nonsurgical treatment of the muscles and tendons of the leg governing the functions of the feet." A. 335 proposes to amend the health and safety code by including a chiropodist in the class of persons who may purchase hypodermic syringes or hypodermic needles or may sign an authorization for such purpose.

Colorado

Bill Introduced.—S. 1 proposes to amend the law concerning vital statistics by making it the duty of the attending physician or midwife to file a certificate of birth within three days after the birth has occurred and setting forth the contents of such certificate.

Delaware

Bill Introduced.—Senate substitute for S. 7 proposes the enactment of a premarital physical examination law. Each applicant desiring to be married would be required to produce a certificate from a physician licensed by the Medical Council of Delaware or a nonresident licensed physician, provided the qualifications of the said nonresident physician are equivalent to those required for license by the Medical Council of Delaware, certifying that he had undergone a thorough physical examination, including a standard serologic test and a darkfield test, if indicated, and stating that in the opinion of the physician the applicant is not infected with syphilis in a communicable stage. The total fee to be paid to any physician by the applicant shall not exceed the sum of $2.50, over and above the fee charged by the laboratory, and the required serologic test may be performed by the Delaware State Board of Health Laboratory or at a laboratory approved for this purpose by the executive secretary of the Delaware State Board of Health.

Georgia

Bill Introduced.—H. 25 proposes the creation of a board of naturopathic examiners to define and regulate the practice of naturopathy. The practice of naturopathy is defined as the science of treating the human body by use of natural methods and shall include the following therapeutic measures: hydrotherapy, psychotherapy, phytotherapy, mechanotherapy, phototherapy, thermotherapy, electrotherapy, biochemistry, and embracing such practices as massage, mineral, thermal, electrical and vapor baths, external application and dietetics. The proposal would exempt from the operation of its terms persons now authorized or hereafter authorized to practice medicine or surgery, chiropractic, osteopathy and chiropody as well as persons engaged in the practice of naturopathy in Georgia at the time of the passage of the bill who were so engaged for at least one year and who were graduates of an accredited naturopathic school. The proposed bill would further authorize naturopaths to use narcotics for the relief of pain and would provide that

naturopaths licensed under the act should observe and be subject to all state, county and municipal regulations in regard to the control of contagious and infectious diseases, with equal rights to use the facilities of the state board of health and to report all births and deaths and to any and all other rights pertaining to the public health in the same manner as is required of other practitioners of the healing arts.

Idaho

Bill Introduced.—H. 24 proposes the enactment of a prenatal examination law. The proposal would require every licensed physician attending a pregnant woman, at the first examination or within fifteen days thereafter, to cause to be taken from such woman a blood sample to be submitted to a laboratory of the department of public health or some other approved laboratory for a standard serologic test for syphilis. In submitting such sample the physician shall specify whether or not it is for a prenatal test or a test following recent delivery. The bill also proposes that persons not permitted to take blood samples, but who do attend pregnant or recently delivered women, must within fifteen days of the first examination cause a sample of blood of such woman to be taken by a licensed physician and submitted as described.

Illinois

Bills Introduced.—S. 24 proposes to amend the pharmacy practice act by limiting to four hours in any one day the time during which any assistant pharmacist shall have the right to act as clerk or salesman in a drug store or pharmacy during the temporary absence of the registered pharmacist. H. 8 proposes the creation of a "Cancer and Tumor Fund" to be used for the treatment of persons afflicted with cancer or tumor and the appointment by the county board of each county of a duly licensed physician familiar with cancer and tumor cases who shall maintain an office in some convenient place during the entire year for the purpose of examining applicants for the benefits of the fund.

Indiana

Bills Introduced.—S. 4 proposes the enactment of a law for the licensing and regulating of nursing homes, defined as any institution for care or treatment of three or more sick, infirm, convalescent, invalid, feeble-minded, mentally ill, incompetent, decrepit, blind, disabled, injured, infected or chronically ill person, drug addict, dipsomaniac or inebriate, and for which care or treatment a charge is made. Exempted from the operation of the bill is treatment in a private household and in any hospital, home or institution conducted by or for the members of any religious body or denomination or regularly organized patriotic, fraternal or charitable organization. Among other things, the bill also proposes that it shall be unlawful to conduct a nursing home unless the treatment and care of inmates in such nursing home are in charge of a registered nurse. S. 7 and H. 29, although not identical bills, propose to amend the workmen's compensation act in certain particulars. Among other things, the bill proposes that an employer shall provide the necessary first aid, medical and surgical services and all necessary medical and hospital services which is reasonably required to cure or relieve the effects of the injuries. Failure of the employee to accept such services would bar the receipt of compensation, and failure of the employer to furnish such services would authorize the employee to consult a physician of his own choice at the employer's expense. An examination of an employee made at the request of the employer shall be performed in the presence of a duly qualified physician or surgeon provided and paid for by the employee, if the employee so desires, and where a physician chosen by the employee is not present the physician engaged by the employer shall furnish the employee with a statement in writing of the conditions evidenced by such examination not later than forty-eight hours before any hearing in the matter is set. H. 66 proposes the enactment of a law regulating the operation of plants for the cold storage of food in individual lockers. Among other things the bill proposes that all employees of such locker plants shall undergo a semi-annual health examination by a physician and requires the employer to keep such health certificates on file at all times. Furthermore the bill proposes to prohibit any person suffering from a communicable disease, including any communicable skin disease or with infected wounds, and any person who is a "carrier" of a communicable disease from being employed in any capacity in such a locker plant. H. 78 proposes the creation of a state board of natural therapeutic physicians to examine and license practitioners of natural therapeutics, such board to consist of six members, including two chiropractors, two naturopaths and two physiotherapists. The bill defines the practice of natural therapy as the diagnosis and treatment of human ailments, by manual and mechanical manipulation and adjusting of the spine and its appendages, the use of herbal remedies, cell salts, diet and the application of heat, cold, air, water, light, electricity, radiant energy and exercise in the treatment of disease, injury or deformity. After passing the required examination a license shall be granted to practice the system or systems for which the applicant is qualified, and the license shall designate the system of natural therapeutics which licensee is permitted to practice. Finally the bill proposes to authorize licentiates thereunder to sign death certificates and execute all legal documents with the same authority as members of any other school or system of healing and proposes to exempt from its operation persons lawfully carrying on their particular profession of healing under any valid existing act of the state, persons rendering gratuitous services in cases of emergency, persons who administer to or treat the sick or suffering by spiritual means or prayer and persons giving baths and massage.

Kansas

Bills Introduced.—H. 25 proposes the granting of temporary licenses to nurses now licensed as such, or who at one time have been licensed as such, outside the state if they are found qualified to practice as nurses in the state during the present war emergency period. Holders of such temporary licenses shall be subject to the same rules and regulations and restrictions as regular licensees. H. 40 proposes to abolish the present state board of medical registration and examination and state board of osteopathic examination and registration, to create a state board of physicians and surgeons registration and examination to be composed of physicians in good standing in their profession who shall have received the degree of doctor of medicine or doctor of osteopathy and to amend the medical practice act in certain particulars so as to include osteopaths under the same terms as physicians and surgeons. Licenses issued by this board would grant the right to practice medicine and surgery and would grant rights to osteopaths equal in every respect to those granted to physicians and surgeons.

Massachusetts

Bills Introduced.—S. 42 proposes the enactment of a law to regulate the sale of apparatus designed as aids to hearing by, among other things, requiring that such sales be made only on prescription of a registered physician who is not in the employ of the seller. S. 62 proposes to authorize the board of registration of nurses, for a period of six months following the taking effect of such proposal, to register without examination any nurse who is a graduate of a training school for nurses satisfactory to the board and who has practiced nursing for a period of five years last preceding the effective date of the act. S. 106 proposes to add a new section to the employment security act providing that payment of benefits shall be made for a period of four weeks prior to the date of birth or delivery of a child and for the four weeks next ensuing after the date of birth or delivery of a child. H. 82 proposes a resolution to the federal manpower commission requesting that public mental hospitals in the state of Massachusetts be classified as a "war industry." H. 87 proposes that before a hospital or sanatorium can be licensed or have its present license renewed it must present a certificate of approval of the egresses, the means of preventing the spread of fire and the apparatus for extinguishing fire, issued by a building inspector of the department of public safety or, in the case of a hospital or sanatorium located in the city of Boston, by a building inspector of said city. H. 88 proposes to amend the law licensing dispensaries or clinics so as to include dental clinics as well as those furnishing medical or surgical advice and treatment and proposes to exempt from the operation of such licensing requirements dental clinics conducted by a licensed maternity hospital. H. 89 proposes to amend the

law licensing clinics and dispensaries by providing that the term "dispensary" shall not include a clinic conducted by a regularly licensed maternity hospital. H. 94 proposes numerous amendments to the food and drug act to make it more nearly conform to the federal food, drug and cosmetic act. Among other things, the proposed bill would provide that a drug sold at retail and containing aminopyrine, barbituric acid, cinchophen, dinitrophenol, sulfanilamide, or their derivatives, or any other drug which has been found by the department to be dangerous to health when used in the dosage, or with the required frequency or duration prescribed, recommended or suggested in the labeling thereof, and so designated by it in a regulation adopted, shall be misbranded unless it is dispensed on a written prescription signed by a member of the medical, dental or veterinary profession who is licensed by law to administer such drug, and its label bears the name and place of business of the seller, the serial number and date of such prescription, and the name of such member of the medical, dental or veterinary profession. It is further proposed that a drug dispensed on a written prescription signed by a member of the medical, dental or veterinary profession (except a drug sold in the course of the conduct of a business of selling drugs pursuant to diagnosis by mail) shall be exempt from the foregoing requirements if the person writing the prescription is licensed by law to administer such drug and if the drug bears a label containing the name and place of business of the seller, the serial number and date of such prescription and the name of such member of the medical, dental or veterinary profession. H. 303 proposes that no health or accident policy which has been in force for a period of three or more years shall be canceled, annulled or renewal refused except for nonpayment of premium or assessment or for good cause shown.

Maryland

Bills Introduced.—H. 46 proposes to amend the workmen's compensation act by requiring the employer to provide medical, surgical or other attendance or treatment, nurse and hospital services, medicines, crutches, apparatus, artificial hands, arms, feet and legs and also to repair or replace eyeglasses which are damaged or destroyed as the result of an accident during the course of the employment. H. 53 proposes to amend the insurance code by exempting from the provisions thereof any policy or contract granting solely and exclusively hospitalization insurance. The present law exempts any policy or contract issued by a non-profit association. H. 59 proposes to amend the workmen's compensation act by redefining the terms "injury," "personal injury" and "accidental personal injury" to include all hernias arising out of and in the course of employment. H. 63 proposes to amend the workmen's compensation act by increasing the compensation to employees suffering from neither total permanent or total temporary disability. H. 80 proposes to amend the workmen's compensation act by increasing the compensation for total loss of hearing of both ears. S. 84 proposes to amend the medical practice act by eliminating the proviso that two courses of medical lectures, both of which shall be either begun or completed within the same calendar year, shall not satisfy the aforementioned requirements. This amendment is apparently for the purpose of enabling graduates of accelerated medical courses to obtain licensure in Maryland. S. 92 proposes the creation by the state board of health of two institutions for the treatment of needy persons requiring medical, nursing or custodial care by reason of chronic illness or infirmity. Admission to such institution shall be on the basis of a statement by a physician and shall be limited to patients who are not suffering from tuberculosis in a transmissible form, mental disease of the type requiring care in a mental hospital, an orthopedic disease of a type admissible to the special orthopedic hospitals, and who are under the age of 16 years. H. 76 proposes to repeal that section of the licensing law providing that no county, city or other political subdivision of the state shall require a license to transact any business or occupation which is required to obtain a state license.

Michigan

Bills Introduced.—S. 9 proposes to amend sections 12883 to 12888 of the Compiled Laws of 1929, providing for free medical and surgical care at the University of Michigan Hospital for certain dependent children. S. 15 proposes the abolition of the office of coroner and the creation of a medical examiner system. The state medical examiner shall be a physician licensed to practice medicine within the state of Michigan and shall possess special training in pathology and the investigation of violent deaths. The board of supervisors of each county in the state would be required to appoint a county medical examiner who shall be a physician licensed to practice medicine within the state and a resident of the county or an adjoining county. The proposal then sets forth the duties of the state medical examiner and the various county medical examiners, among which is the duty, on the part of the state medical examiner, to organize, equip and conduct a laboratory to facilitate the carrying out of the purposes of the act. H. 40 proposes to amend the existing premarital examination law by providing that no such examination shall be required of persons serving in the armed forces of the United States during the continuation of the war.

Nebraska

Bills Introduced.—Bill No. 40 proposes the requirement of a premarital examination by each applicant for a marriage license. The necessary certificate shall be signed by a duly qualified physician licensed to practice medicine and surgery in any state or United States territory and shall certify that the applicant is not infected with syphilis in a communicable stage. Bill No. 41 proposes the enactment of a prenatal examination law. This bill would require every physician attending a pregnant woman to take a sample of blood of such woman at the first examination and submit such sample to an approved laboratory for a standard serologic test for syphilis. In reporting every birth and stillbirth, physicians and others required to make such reports shall state on the certificate whether a blood test for syphilis has been made on a specimen of blood taken from the woman who bore the child, but the birth certificate shall not show the result of such test.

New Jersey

Bill Introduced.—A. 41 proposes to amend the medical practice act by repealing chapter 115 of the laws of 1939. That law was a general amendment to the medical practice act making uniform the requirements for a license for all persons who practice any branch of medicine or surgery or use any method of treatment of human ailment, disease, pain, injury, deformity, mental or physical condition except certain enumerated classes of persons already licensed within the state.

Ohio

Bills Introduced.—S. 13 proposes to amend the law relative to privileged communications by providing that a physician may testify by express consent of the patient or if the patient is dead by express consent of the executor or administrator of the patient and by providing further that if the executor or administrator of a patient voluntarily testifies the physician may then be compelled to testify on the same subject. S. 17 proposes to exempt from the operation of the sales tax the sale of drugs or medicine compounded, prepared or sold in accordance with or under a prescription issued by a licensed practitioner of medicine.

Rhode Island

Bill Introduced.—H. 533 proposes the creation of a special commission, to be known as the Special Rhode Island Public Health Laws Survey Commission, to make a comprehensive reexamination and survey of the public health laws of the state and municipalities thereof and to make recommendations for complete modernization of those laws in keeping with the most recent innovations and tried practices of other states. Such recommendations must be made in legislative form not later than April 12, 1943.

South Carolina

Bill Passed.—S. 17 passed the Senate on January 21. This bill proposes to eliminate, from the educational requirements of physicians stated in the medical practice act, the requirement that the necessary four full courses of lectures of at least twenty-six weeks each must have been given in four different years. The purpose of this proposal, apparently, is to enable graduates of accelerated medical courses to obtain licensure in South Carolina.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

DISTRICT OF COLUMBIA

Society Aids in Low Cost Care for Federal Women Workers.—The Medical Society of the District of Columbia is cooperating with the U. S. Public Health Service in providing low cost medical care to the women who will occupy the four new dormitories scheduled for early completion by the government, according to the Washington *Daily News*, January 20. Under the program, private physicians still will operate independently and bill their patients separately but will base their fees on a special low priced schedule agreed on for workers making less than $1,620. Infirmaries will be set up in each of the four dormitories, in charge of a chief nurse and an assistant to be paid out of public funds. They will give girls free infirmary care for minor illnesses and will present each girl with a medical society panel list of physicians from which to choose should she require care. The medical societies of Prince Georges and Arlington counties and the Medical and Chirurgical Faculty of Maryand are also cooperating in the project. Office space will be provided for physicians at each dormitory. Arlington Farms with six residence halls accommodating about 600 women will have a sixty bed infirmary; West Potomac Park, with three halls, a sixty bed infirmary; Langston Stadium for Negro girls, a 12 bed infirmary, and Suitland will have accommodations for six beds. The plan was developed by the public health service, which anticipates that the infirmaries will take some of the load off hospitals, it was stated.

ILLINOIS

Suits Against State Officials Dismissed.—The U. S. Circuit Court of Appeals ruled on Dec. 15, 1942 that private citizens may not sue state officials to recover damages alleged to have been sustained through official acts, newspapers reported. The decision was handed down in suits against A. L. Bowen, Springfield, former state director of public welfare; Mrs. Blanche Fritz, former assistant director; Dr. Albert C. Baxter, Springfield, former state director of public health, and Dr. Ralph T. Hinton, Payson, former superintendent of the Manteno State Hospital, Manteno. The suits grew out of a typhoid epidemic at the hospital in 1939, when a number of persons died.

Chicago

Memorial Service for Physician Who Died in Military Service.—The Chicago Medical Society sponsored a memorial service in the Sauganash Community Church, January 10, for Major Lemuel Edward Day, M. C., U. S. Army, who "died in a New Guinea field hospital, December 23, 1942, two days after he had won the silver star for heroism in a bombing raid on his hospital." Major Day was a first lieutenant in the field artillery in World War I. He joined the army again last June.

Branch Meetings.—Dr. Dallas B. Phemister will address the North Shore Branch of the Chicago Medical Society, February 2, on "Prevention and Treatment of Surgical Shock." At a meeting of the North Suburban Branch, January 11, Drs. Paul S. Rhoads and Samuel J. Lang, Evanston, Ill., discussed "Nonspecific Pneumonia: Report of 100 Cases" and "Adrenal Cortical Insufficiency and Its Treatment" respectively. At a joint meeting of the South Chicago and South Side branches, January 14, the speakers were Drs. Daniel H. Levinthal on "Surgery of Derangements of the Knee Joint" and Sidney A. Portis, "Modern Treatment of Liver Disease." The Northwest Branch was addressed, January 15, by Drs. Frank F. Maple and Charles H. Phifer on "Bleeding in the Third Trimester" and "Procurement and Assignment for Physicians" respectively. The Douglas Park Branch devoted its meeting, January 19, to a showing of a new motion picture film on peptic ulcer. The Jackson Park Branch was addressed on January 21 by Dr. M. Edward Davis on "The Therapeutic Role of the Estrogens in Gynecologic Practice." John F. Svoboda, D.D.S., spoke on "Oral Lesions of Interest to the General Practitioner" at a meeting of the West Side Branch, January 21. A joint meeting of the Englewood and Stock Yards branches was addressed, January 21, by Dr. Karl A. Meyer on "Surgery of the Colon Exclusive of the Rectum." The Aux Plaines Branch was addressed, January 22, by Dr. Harold O. Jones on "Office Gynecology." Dr. Italo F. Volini spoke on "Pneumonia—Typical and Atypical Types," before the Calumet Branch, January 22.

INDIANA

Examination of Applicants for Reciprocity Suspended.—At a meeting, January 12, the Indiana State Board of Medical Registration and Examination passed a resolution to suspend the practical examination for reciprocal applicants for the duration. It was also decided to suspend the requirement of one year's practice in the original licensing state for reciprocal applicants. The board also changed the regulation for graduates located outside the United States and possessions to read "outside of the United States and its possessions, and outside the Dominion of Canada for the duration. . . ."

Dr. Stayton Retires as Editor of Bulletin.—Dr. Chester A. Stayton, Indianapolis, has retired as editor in chief of the Indianapolis Medical Society Bulletin, a position he had held since he established the bulletin in its present form in June 1931. Mr. Russell Campbell, secretary to Mayor Sullivan of Indianapolis, is the new editor in chief on a part time basis. Prior to its establishment in its present form the bulletin was published weekly as a post card. Dr. Stayton, who was then secretary of the society, continued the new bulletin with the volume number that had been carried by this weekly card.

Physician Recommended for Navy Cross.—Dr. Don M. Mattox, Terre Haute, lieutenant (j. g.), M. C., U. S. Navy, has been recommended for the Navy Cross and cited for decorations by both navy and army commands as a result of service rendered during the invasion of French Morocco, according to the state medical journal. Dr. Mattox entered the service on July 16, 1942 and was first assigned to duty with the U. S. Marine Corps at Parris Island, S. C. Later he was transferred to the amphibious forces of the navy and served with the naval medical units on the African beaches in the vicinity of Casablanca during the invasion which began on November 7.

MARYLAND

One Case of Smallpox Breaks Twelve Year Record.—The occurrence of a mild case of smallpox in St. Mary's County has broken a record of twelve years without a report of the disease. The case was traced to an Amish minister who had visited the Amish area in Pennsylvania, where an outbreak had occurred in December (THE JOURNAL, January 2, page 61). The minister had visited Charles and St. Mary's counties. Vaccination of all known contacts was under way within one hour after the information was received. All those known to have been exposed to the disease were vaccinated except one man, who was not vaccinated until December 28. It was this man who developed a mild case of smallpox. Regular vaccination clinics are being conducted in localities where contacts and cases have come into Maryland from the parts of Pennsylvania where the disease had occurred.

Premedical Study Reduced at University of Maryland.—The faculty of the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, has agreed to reduce the period of premedical study for admission to two academic or scholastic years, or their equivalent, consisting of not less than sixty semester hours, provided the minimum number of semester hours of instruction in the prescribed basic subjects for a premedical education is included, exclusive of physical education and military science, in an approved college of arts and sciences. This is in conformity with the recommendations of the Association of American Medical Colleges and the Council on Medical Education and Hospitals of the American Medical Association. The reductions in admission requirements are to continue in force until further notice. The decision was made following the adoption of resolutions recommending the action by the Association of American Medical Colleges and the Council on Medical Education and Hospitals of the American Medical Association.

Dr. Streeter Honored.—To mark his many years of service to the Carnegie Institution of Washington, volume 30 of the Contributions to Embryology, which appeared Dec. 31, 1942, was dedicated to Dr. George L. Streeter, Baltimore, who was director of the department of embryology at the institution from 1918 to 1940 and chairman of the division of animal biology from 1935 to 1940, when he became research associate. The tribute also recognizes the work of Dr. Streeter in serving as editor of the volumes 8 to 29 during the period 1917 to 1940. *Science* reports that it is customary, when such an achievement is to be honored, to assemble a testimonial volume of especially written articles. Dr. Streeter's colleagues chose, however, to convey their tribute by means of a regular volume

of the series prepared in the usual course of scientific research, thinking that in this way they might best call attention to the fact that the whole series is a testimonial to Dr. Steeter. This volume represents workers of ten laboratories in three continents. Most of the investigations were carried out in the Carnegie Embryological Laboratory and all except one made use of its collections or other facilities. It is dedicated to Dr. Streeter in the name not only of the present contributors but of all those investigators now scattered over the Americas, Europe and Asia, many of them inaccessible or distracted by reason of the war, who have worked in this laboratory and published their results under his editorship. The volume also contains an article prepared by Dr. Streeter testifying to his eminence as investigator as well as editor. Dr. Streeter was born in Johnstown, N. Y. He graduated at Columbia University College of Physicians and Surgeons, New York, in 1899. He was demonstrator in anatomy of the nervous system at Albany Medical College, 1901-1902; later he served as assistant and instructor in anatomy at Johns Hopkins University School of Medicine, Baltimore, and assistant professor of anatomy at the Wistar Institute of Anatomy and Biology at the University of Pennsylvania, Philadelphia. He was professor of anatomy and director of the anatomy laboratory at the University of Michigan Medical School, Ann Arbor, from 1907 to 1914, when he went to the Carnegie Institution as research associate. A member of many national scientific societies, Dr. Streeter was president of the American Association of Anatomists in 1926. His research has been concerned with human embryology, development of the central nervous system, the internal ear and experimental biology.

MICHIGAN

Program to Conserve Hearing.—The Michigan Department of Health and the state department of public instruction are cooperating in a new program especially planned to help hard of hearing children. The program aims to discover actual and potentially hard of hearing children. Medical attention will be arranged and educational opportunities offered for both the children and the parents. Audiometric hearing tests will be given by the state department of health.

District Units for Industrial Hygiene.—Two new district offices have been set up by the state bureau of industrial hygiene, bringing the total of such district units to five. One new unit is located in the Kalamazoo City-County Department of Health, with facilities for Kalamazoo, Van Buren, Berrien, Cass and St. Joseph counties. The second unit in the Washtenaw County Health Department in Ann Arbor serves Washtenaw, Jackson, Hillsdale and Lenawee counties. Other units are located in Grand Rapids, Saginaw and Pontiac.

Victory Day Clinic.—The staff of Mount Carmel Mercy Hospital, Detroit, held a "victory day clinic" January 27. Participating in the clinic were:

Drs. Harold L. Morris and Samuel A. Flaherty, Detroit, Urology.
Dr. William L. Bendel, Monroe, La., Pelvic Inflammatory Disease: Treatment and Its Course.
Dr. Carl E. Badgley, Ann Arbor, Treatment of Colles' Fracture.
Dr. William Reid Morrison, Boston, Certain Aspects of the Problems of Gastric Surgery.
Dr. Charles F. McKhann, Ann Arbor, Neonatal Care.
Dr. Edgar H. Norris, Detroit (subject not announced).
Dr. Albert C. Furstenberg, Ann Arbor, Diseases of the Salivary Glands.
Dr. Fay A. Le Fevre, Cleveland, Treatment of Coronary Heart Disease.
Dr. Irving W. Potter, Buffalo, Why We Do Podalic Version.

NEW YORK

The Lucien Howe Prize.—The Medical Society of the State of New York announces that all essays for the Lucien Howe Prize must be received by the chairman of the committee on prize essays of the society, Dr. Charles G. Heyd, 292 Madison Avenue, New York, not later than March 1. One hundred dollars will be presented for the best original contribution on some branch of surgery, preferably ophthalmology, during the annual meeting of the medical society in Buffalo in May.

Plasma Education Program.—A graduate medical education program in the indications for and technics of using blood plasma is being prepared by the state medical society, Office of Civilian Defense and the state department of health and will be launched soon through the medical society's committee on public health and education. Plans are being patterned after the recent method of handling and treatment at the Massachusetts General and Boston City hospitals after the Cocoanut Grove disaster. According to *Health News*, one of the hospitals was fortunate in having not only a complete "burn unit" organized in advance of the disaster but also a trained technical team. At the other hospital a similar unit was in process of organization and, although not completed at the time of the fire, the progress that had been made was clearly reflected in the expeditious manner with which it was possible to care for the tremendous number of injured persons in a very short time. Dr. Earle B. Mahoney, who is in charge of the blood plasma unit at Strong Memorial Hospital, Rochester, and who is serving as consultant to the state department of health, and Dr. Edward S. Rogers, Albany, assistant commissioner for medical administration on the department's staff, studied the Boston situation shortly after the disaster.

Dr. Calkins Dies.—Gary N. Calkins, Sc.D., professor emeritus of protozoology at Columbia University, New York, died in Scarsdale, January 4, aged 73. After graduating in 1890 at the Massachusetts Institute of Technology, Boston, Dr. Calkins was for the next three years assistant biologist to the Massachusetts Department of Public Health and a lecturer in biology at the institute. In 1894 he was made a tutor in zoology in the newly organized zoology department at Columbia, in 1903 assistant professor of zoology and in 1904 a full professor. Three years later he became the first professor of protozoology, retiring in 1939 as professor emeritus. From 1903 to 1908 he was biologist for the New York State Cancer Laboratory, Buffalo, and since 1937 had been a member of the Columbia Consulting Board for Cancer Research. During his many years at Columbia Dr. Calkins had also taught parasitology and gave the invertebrate half of the general undergraduate course in biology. From 1928 to 1931 he was executive officer of the department of zoology at Columbia and in 1935, while on sabbatical leave, delivered a series of lectures at the School of Tropical Medicine of Puerto Rico University, San Juan. Dr. Calkins was a member of numerous scientific organizations and from 1913 to 1914 was president of the American Society for the Control of Cancer and from 1919 to 1921 of the Society of Experimental Biology and Medicine.

New York City

Public Welfare Commissioner Killed in Airplane Crash.—William Hodson, LL.B., commissioner of public welfare, who had been carrying out a mission for Herbert H. Lehman, LL.D., federal director of foreign relief and rehabilitation, was killed in an airplane accident in Paramaribo, Dutch Guiana, January 15. Mr. Hodson recently completed his ninth year of service as commissioner of public welfare and had been granted a two months leave of absence to undertake a mission for former Governor Lehman.

Bacteriologist Dies.—Frederick Dixon Chester, bacteriologist and chemist, died at his home in the Bronx, January 1, aged 82. Dr. Chester was born in Santo Domingo, Haiti, in 1861. He received his M.S. degree at Cornell University, Ithaca, N. Y., in 1885. He had served as professor of geology and botany at Delaware College, bacteriologist and mycologist, Experimental Station, Delaware, and director of the Delaware State Bacteriological Laboratory. He was a consulting chemist and bacteriologist from 1907 to 1924, when he became the chief chemist of the Stackpole Carbon Company in Pennsylvania, a position he left in 1930 to become director of research of the Technical Sales Corporation.

Course in Industrial Medicine and Surgery.—Columbia University announces a postgraduate course in industrial medicine and surgery to be held February 1-13. Members of the faculty of medicine, the De Lamar Institute of Public Health and visiting lecturers will conduct the series. Among the speakers will be:

Dr. McIver Woody, Organization of an Industrial Medical Service.
Dr. John J. Wittmer, Industrial Absenteeism.
Dr. Leroy U. Gardner, Saranac Lake, N. Y., Silicosis, Asbestosis and Other Dust Diseases.
Dr. George M. MacKee, Industrial Dermatoses.
Frederick B. Flinn, Ph.D., Poisoning Due to Metals Other Than Lead.
Dr. Wolfgang F. von Oettingen, Bethesda, Md., Poisoning Due to Gases.
Helmuth H. Schrenk, Ph.D., Pittsburgh, Poisoning Due to Hydrocarbons.

Report Shows Increase in Venereal Disease.—A "serious rise" in venereal disease was noted for 1942, according to the annual report of the city health department. For the first eleven months of the year there were 28,068 cases of syphilis recorded, an increase of 13 per cent over the corresponding period of 1941. A total of 11,208 cases of gonorrhea was reported, with the number of unreported cases thought to be many times greater, according to the New York *Times*. Neither venereal disease nor any other vital statistics of service men on duty are included in the city reports. The birth rate was 17.4 per thousand estimated population in 1942, the highest since 1930, when it reached 17.7. An all time low was noted in the city's infant mortality rate of 28.8 for 1,000 live births. The general death rate was 10 per thousand of estimated population. The rate for tuberculosis was 46.3 per hundred thousand and that for pneumonia 39.1. Seven deaths from diphtheria were recorded as against ten in 1941, 90 cases

and nine deaths from infantile paralysis, and 437 from appendicitis, giving a new low rate from this cause of 5.8 per hundred thousand. Accidents caused 3,643 deaths, accounting for a rate of 48.1 per hundred thousand.

NORTH CAROLINA

Report of Society. — The Buncombe County Medical Society, in a report of its activities for the past year, announces its decision to discontinue publication of its monthly bulletin and to hold only one meeting a month for the duration of the war. Among other activities, the society aided in advancing the development of a hospital for Negroes at Asheville, organized a blood plasma bank, and turned its management over to the city health department. It sponsored weekly radio talks by members. Thirty-six members of the society, being just one third of the active membership, are now serving with the armed forces of the United States.

OHIO

Department of Physical Medicine Created at State University.—The establishment of a department of physical medicine at the Ohio State University, Columbus, with quarters on the first floor of University Hospital, has been announced. Dr. David E. Jones, clinical assistant in orthopedic surgery, University of Louisville School of Medicine, Louisville, Ky., has been placed in charge of the new department.

Industrial Health Program Formulated.—Recommendations for an active industrial health program in Ohio were recently approved. They were submitted in a report of the newly formed committee on industrial health of the state medical association and are to form sound local educational programs on industrial health designed to curtail absenteeism of workers, especially in war industries, because of sickness and injury, to eliminate health hazards in plants, to educate workers and their families to keep themselves in good health, to encourage good health and medical services for employees, and to provide educational opportunities for members of the medical profession on matters of industrial health and the care of those disabled as a result of employment. The establishment of state and local organizations within the medical profession to carry out these objectives was also recommended. Dr. Barney J. Hein, Toledo, is chairman of the new committee on industrial health, and other members are Drs. David W. Heusinkveld, Cincinnati, Herbert M. Platter, Columbus, George F. Sykes, Cleveland, Ernest O. Swartz, Cincinnati, Ralph M. Watkins, Cleveland, Orville J. Walker, Youngstown, Carl A. Wilzbach, Cincinnati, and the president, president-elect and past president of the state medical society, ex officio.

RHODE ISLAND

Midwinter Meeting of the State Medical Society.—The Rhode Island Medical Society will hold a special midwinter meeting at the Medical Library, Providence, February 4. Dr. James E. Paullin, Atlanta, Ga., President-Elect of the American Medical Association will discuss "The Contribution of the Physician in the Present Crisis." Other speakers will be Drs. James C. McCann, Worcester, Mass., and Herman C. Pitts, Providence, on "Prepaid Medical Care and the National Outlook" and "The Rhode Island Cash Sickness Act" respectively.

TEXAS

Hospital Group Plans War Conference. — The Texas Hospital Association will conduct a war conference, February 18-19, at the Hotel Texas, Fort Worth. Among the speakers will be James A. Hamilton, New Haven, Conn., president of the American Hospital Association. Other speakers will include Major James H. Stephenson, U. S. Public Health Service, on "Civilian Defense in Hospitals"; F. Hazen Dick, Louisville, Ky., and Everett W. Jones, B.S.E., Washington, D. C., "Hospital Purchasing in Wartime," and Russell L. Dicks, Dallas, "Psychosomatic Medicine and Its Implications for the Treatment of the Patient." Other groups meeting at the same time are the Association of Records Librarians of Texas, Texas Association of Nurse Anesthetists and the Texas Association of Hospital Accountants.

VIRGINIA

Courses on Industrial and Military Medicine. — The state medical society is preparing a series of graduate courses on industrial and military medicine to be given in various sections of Virginia. The program will provide for afternoon, dinner and evening meetings in each of five centers comprising a circuit of a week. According to present plans the courses will begin the latter part of February or early in March with from three to five speakers on each program.

WISCONSIN

Personal.—Dr. Edwin Hall Jorris, Madison, supervisor of local health services and director of the division of tuberculosis control of the Wisconsin State Board of Health, has been commissioned a lieutenant commander in the medical corps of the U. S. Naval Reserve.

Information Please Program on Therapeutics. — The Medical Society of Milwaukee County devoted its meeting, January 8, to an "information please" program. Therapeutics was the theme of the program, and Drs. Edward H. Rynearson, Rochester, Minn., Ovid O. Meyer, Madison, Francis D. Murphy, Frederick W. Madison and Theodore L. Squier, Milwaukee, constituted the board of experts.

Dr. Harper Retires After Thirty-Nine Years as Health Officer.—Dr. Cornelius A. Harper, Madison, retired on January 28 as state health officer, a position he has held since April 1, 1904. He has been a member of the board since February 1901. Dr. Carl N. Neupert, Madison, who has been assistant state health officer for six years, has been named secretary to the board of health and state health officer. Dr. Harper has been named medical specialist in public health to the state board. He graduated at the Columbian University Medical Department, Washington, D. C., in 1893.

GENERAL

Women Over Thirty Urged to Have More Babies.—According to statisticians of the Metropolitan Life Insurance Company American women of 30 and over must have more babies if the present high birth rate is to be maintained. The withdrawal of large numbers of men for military service will result in a decrease in births among younger women, it is pointed out. In the case of women of ages 30 and over, the contribution to total annual births was smaller at the end of the last two decades than at the beginning. In 1920 their contribution was 35 per cent of the total births as against 29 per cent of the total babies born in 1940. Most married women of these ages already have children so that their husbands are, for the most part, still out of the classes called for military service, it was stated. In addition, thousands of these families are now in a better economic position than ever to rear more children.

New Motion Picture on Sulfonamide Therapy.—A new motion picture on sulfonamide therapy was recently released by Lederle Laboratories, Inc., and is available for bookings without charge to medical groups. The film was prepared by and under the supervision of Drs. Norman H. Plummer, assistant professor of clinical medicine at Cornell University Medical College, New York, and Charles H. Wheeler, assistant in pharmacy (therapeutics) at Cornell. The film reviews the development of the sulfonamides from 1908 to the present time. The chemical aspects are shown in scenes taken at the sulfonamide research division of the Lederle Laboratories, and therapeutic applications are revealed in scenes taken at the New York Hospital. By special arrangement Drs. Edward F. Roberts, New York, and Florian E. Schmidt, Chicago, will present the film with comments, or the film may be borrowed by medical societies or hospital staffs.

Mr. Fieser's Work Expanded for Red Cross. — Mr. James L. Fieser, Washington, D. C., who has been vice chairman in charge of domestic operations of the American Red Cross since 1922, has become vice chairman at large, in accordance with organization changes made to meet the expanding activities of the national group. Mr. Fieser will report to the chairman and will assist the chairman and the operating departments and services in relations with the many national organizations which are becoming increasingly important to the Red Cross, will assist with the War Fund Campaign, will be available for such special assignments and for attendance at such meetings as may be requested by the chairman, and will be of assistance to the operating departments and services. The department of domestic operations will report to the executive vice chairman, Mr. Lloyd B. Wilson, Washington, D. C., who will assume this responsibility in addition to his other duties.

Walter Reed Medals Presented.—The American Society of Tropical Medicine presented two Walter Reed medals during its recent annual meeting in Richmond in November. One was presented to the United States of Brazil through its minister of education and public health, Dr. Gustavo Capanema, Rio de Janeiro, for outstanding work in eradicating Anopheles gambiae from Brazil. In the absence of Dr. Papanema, Dr. Mario Kroeff, Rio de Janeiro, director of National Cancer Service, received the award. The second medal was presented posthumously to Dr. Carlos J. Finlay for pioneer work in yellow fever. Dr. Finlay's son, Dr. Carlos E. Finlay, was to

have received the medal, but because of his illness it was received by Dr. Domingo F. Ramos, director of the Finlay Institute, Havana. Dr. Wilbur A. Sawyer, N. Y., was chosen president-elect of the American Society for Tropical Medicine and Dr. N. Paul Hudson, Columbus, Ohio, was installed as president. Rear Admiral Charles S. Stephenson, M. C., U. S. Navy, is vice president; Col. Charles F. Craig, San Antonio, Texas, editor, and Dr. Joseph S. D'Antoni, New Orleans, secretary-treasurer.

Grants Available by Ella Sachs Plotz Foundation.—The Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation announces that, during the present great need for funds, forthcoming grants will be given in the sciences closely related to medicine without reference to special fields, a policy somewhat neglected in the past. The maximum size of grants will usually be less than $500. Applications for grants to be held during the year 1943-1944 must be received by the executive committee before April 1943. There are no formal application blanks, but letters asking for aid must state definitely the qualifications of the investigator, an accurate description of the research, the size of the grant requested and the specific use of the money to be expended. Applicants should also state whether or not they have approached other foundations for financial assistance. Applications should be sent to Dr. Joseph C. Aub, Massachusetts General Hospital, Fruit Street, Boston. In its nineteenth annual report the Ella Sachs Plotz Foundation stated that twenty-six grants were made during the past year, one being a continued annual grant. Forty-four applications for grants were received by the trustees, thirty-six of which came from the United States, the other eight coming from six different countries in Europe, Asia and North and South America. The foundation has distributed four hundred and fifty-five grants to scientists throughout the world during its nineteen years' existence.

Prize for Research on Problems of Alcohol.—The Research Council on Problems of Alcohol has announced the establishment of a $1,000 award for outstanding research on alcoholism during 1943. The research must contribute new knowledge in some branch of medicine, biology or sociology important to the understanding or prevention or treatment of alcoholism. The project may have been inaugurated at any time in the past or during the year, provided that a substantial part of the work is carried on during the year, that it is developed to a point at which significant conclusions are possible before the end of the year and that a report on the work has not been previously announced and described before a scientific body or previously published. It is desirable, but not necessary, that those planning to work for the award send to the council before March 1 a statement of such intention. If the council receives such information, it can be helpful in the prevention of undesirable duplication of effort. If a research project is conceived and inaugurated later in the year, a statement of intention may be sent to the council at a later date. A report on the work and resulting conclusions must be submitted to the Research Council on Problems of Alcohol on or before Feb. 15, 1944. The council will provide an outline for use in the preparation of reports. The award will be in cash and will be given to an individual scientist whose work is judged sufficiently significant to merit the award. The committee of award will consist of five persons—an officer of the American Association for the Advancement of Science and four representatives of the scientific committee of the Research Council on Problems of Alcohol. Any scientist in the United States, Canada or Latin America is eligible for the award. The council will send on request to any scientist an outline of basic policies governing its research program, lists of council studies (completed, under way and contemplated), and information regarding the studies of other agencies. Scientists planning to do research in connection with the award may send a statement of intention to the director, Research Council on Problems of Alcohol, 111 Pondfield Road West, Bronxville, N. Y.

LATIN AMERICA

Personal.—Drs. Jorge Millan Gutierrez, Mexico, was recently chosen president of the Sociedad Mexicana a Dermatologia of Mexico City; Pedro Daniel Martinez was elected secretary and Robert Nunez Andrade treasurer.

Medical Congress Marks Anniversary Centennial.—The first National Congress of Medicine was held at the University of Chile, Nov. 17-21, 1942, under the direction of the faculty of biology and medical sciences of the university, as a part of the centennial celebration of the university. The University of Chile was founded on Nov. 19, 1842. According to the *Revista Medica de Chile*, October 1942, it is deplored that the world conflict restricted the participation of medical men of North America.

FOREIGN

Royal College of Physicians.—The annual meeting of the Royal College of Physicians of Edinburgh was held Dec. 3, 1942. Dr. Charles McNeil was reelected president and Drs. Lewis H. F. Thatcher, Alexander Murray Drennan, Andrew Fergus Hewat, David M. Lyon, Andrew Graham Ritchie and Andrew Rae Gilchrist were elected to form the council of the college for the ensuing year. Dr. Hewat was nominated vice president.

Scientists Honored.—Sir Robert Robinson, D.Sc., Oxford, authority on organic chemistry, recently received the Copley Medal of the Royal Society. Sir William Wilson Jameson, formerly dean of the London School of Hygiene and Tropical Medicine and now chief medical officer to the Ministry of Health and the Board of Education, London, received the Buchanan Medal for "administrative and constructive work" of outstanding merit in the service of hygienic science. Other awards of the society went to Prof. Walter N. Haworth, D.Sc., Birmingham, for his work in organic chemistry and Dr. William W. C. Topley, London, for his studies in bacteriology. The awards were announced by Sir Henry H. Dale, C.B.E., fullerian professor and director of the laboratories of the Royal Institution, London, and president of the Royal Society, in an address commemorating the three hundredth anniversary of the birth of Isaac Newton.——Dr. Alfred Vogt, professor of ophthalmology at the University of Zurich, Switzerland, since 1923, has been presented with the Gullstrand Medal by the Swedish Medical Society of Stockholm. The medal is awarded every ten years to an eminent ophthalmologist, *Science* reports.——Professor Von H. Mooser, director of the Institute of Hygiene of the University of Zurich, has been elected an honorary member of the Royal Academy of Medicine of Barcelona for his researches on typhus fever recently made in Spain.

CORRECTIONS

The Typhoid Carrier State Treated with Sulfaguanidine.—In the clinical note by Major Robert J. Hoagland in THE JOURNAL, Dec. 12, 1942, page 1211, the dose of sulfaguanidine used by Levi and Willen should have been written as 0.05 Gm. per kilogram of body weight instead of 0.5 Gm.

Protective Ointment for Welders.—In a Query and Minor Note entitled "Erythema from Welding" published in THE JOURNAL, January 9, page 162, an ointment for the protection of welders was suggested which would consist of zinc oxide ointment to which is added 10 per cent tannic acid or 5 per cent methyl salicylate. This should be menthyl salicylate, as should a similar reference below it.

Government Services

Urge Speedy Naturalization of Alien Physicians

Because of the acute shortage of civilian physicians throughout the United States, the Immigration and Naturalization Service has been directed to expedite the naturalization of alien physicians, according to a release from the Department of Justice, January 16. Immigration Commissioner Earl G. Harrison has issued instructions to expedite the filing of petitions for naturalization and to hold hearings in advance of their regular order on the calendar in the cases of practicing alien physicians or aliens who would be qualified to practice if they were citizens. In issuing the instructions, Commissioner Harrison pointed out that many states, either by statute or by the administrative ruling of licensing boards, require applicants to establish American citizenship before they are admitted to the state licensing examinations for the medical profession. Other states, he said, issue temporary licenses which are subject to cancellation unless citizenship is obtained within a specified period of time. The order expediting naturalization of physicians supplements instructions issued the service in January 1942 to expedite applications for citizenship submitted by aliens in the armed forces or engaged in national defense work. In the case of physicians they are not required under the new instructions to obtain a letter from a national defense agency testifying to the nature of their employment in order to secure national defense preference in naturalization. Attorney General Francis Biddle emphasized that the new procedure in no way affects the statutory requirements for naturalization but simply expedites the handling of applications.

Foreign Letters

BRAZIL

(From Our Regular Correspondent)

Dec. 5, 1942.

Neurosyphilis and Delinquency

The high incidence of syphilis, particularly neurosyphilis, in criminals in Rio de Janeiro was emphasized some time ago by Dr. Cerqueira Luz, who found that the percentage of positive Wassermann tests in the blood of criminals in a large penitentiary (Casa de Detenção) was much higher than that of patients in the hospitals of the city, even those with a special clinic for neurosyphilis. In a recent paper Dr. Heitor Carrilho reports a study of 600 inmates of a hospital for the criminal insane (Manicomio Judiciario). The study disclosed that 134 of them (22¼ per cent) had a positive Wassermann reaction in the blood. There was no especial difference in the percentage of positivity of the test in the blood among criminals according to the different types of delinquency: 19.7 per cent in crimes against persons, 24 per cent in crimes against property and 24 per cent in misdemeanors. The Wassermann test of the cerebrospinal fluid has been carried out on 500 inmates of the Manicomio Judiciario, 37 of them (7.4 per cent) having been positive. In this instance the percentage of positives is significantly different in the various classes of delinquency: 3.5 per cent in crimes against persons, 11.4 per cent in crimes against property and 8.6 per cent in misdemeanors. But these 37 cases do not represent all the instances of abnormality of the central nervous system among these persons. When all the various tests performed with the cerebrospinal fluid of the 500 inmates, i. e. the Wassermann reaction, the globulin reactions, the colloidal reactions and the cell count, are taken together, there are 277 cases in which one or more of these tests have been positive, showing that 55.2 per cent of the patients had inflammatory changes of the central nervous system, which strongly suggests neurosyphilis. In several cases of relapsing delinquency the repetition of the examination clearly demonstrated the presence of syphilis. Dr. Carrilho points out that the problem of relapsing delinquency finds in numerous cases an explanation which is well within the province of neuropsychiatry.

The Health of Children of Persons Afflicted with Leprosy

In a recent paper Dr. Octavio Gonzaga and others of the Division of Leprosy of the São Paulo State Department of Health reported a survey of the health of children of leprous patients inmates of the St. Teresinha Preventorium, founded in 1927. The institution at Carapicuiba, about 18 miles from the city of São Paulo, harbors 250 children from a few months to 13 years of age whose parents have leprosy and are now isolated in the state leprosariums. Among 73 deliveries at the maternities of these leprosariums during the year 1941 there were 9 stillbirths (12.3 per cent). The authors report a high morbidity and mortality rate for the children of the leprous living in the crowded nurseries of the leprosariums (20 annual deaths per hundred infants received at the nurseries just after birth). The necropsy of 20 of these infants disclosed that 18 had died from acute infections of the respiratory tract, 1 from purulent meningitis and 1 from obstetric trauma. Many of the newborn have congenital debility, 85 per cent of them being under 7 pounds (3.2 Kg.) at birth and 25 per cent under 5 pounds (2.3 Gm.). The state of debility is much more common among the children from mothers affected with the lepromatous form of the disease than the ones from mothers with the pure nervous form. The leprosy of the fathers does not cause congenital malformations and degenerations among the children, who are normal in reference to stature, weight, morbidity and mortality rates, without any particular feature that may be related to a specific character of the father. No case of transplacental leprosy has been disclosed up to this date. In the careful observation of 300 children from leprous parents, isolated just after birth up to the age of 13, as well as in 51 necropsies, the so-called congenital leprosy has been so rare that the authors believe this expression may be considered meaningless. Among the 51 necropsies only 1 case presented a small papulous lesion of the face, but the suspicion of leprosy was not confirmed by the careful examination of all the organs. In another case a large Ghon pulmonary focus and tuberculous lymphangitis made the search for the Hansen bacillus useless, owing to the concomitant tuberculous infection. The authors believe that the isolation of the children from the leprous parents just after birth is sure protection against the later appearance of the disease.

When they are infected a short time after birth the infants present a high resistance to the disease. The authors think that the relatively mild course of the leprosy in children of tender age may be explained by the existence of an "extinct precocious leprosy" rather than by any natural individual resistance. In a majority of the cases the infant leprosy is of the mild tuberculoid type with a tendency to spontaneous cure. In the preschool and school ages, on the contrary, the disease frequently takes a malignant character with a tendency to generalization. The use of the Mitsuda test on the children in the preventoriums is very useful in disclosing the state of specific immunity to leprosy.

Personal

Dr. Olinto de Oliveira, professor emeritus of pediatrics of the Porto Alegre University and director of the National Department of the Child of Brazil, has been elected an honorary member of the Society of Pediatrics of New York. At the recent meeting of the South American Confederation of Pediatric Societies at Buenos Aires Prof. Araoz Alfaro of that city proposed to bestow on Professor Olinto de Oliveira the special title of "Dean of the South American Pediatricians," which was approved unanimously.

Marriages

WENDELL PHILLIPS STAMPFLI JR., Monahans, Texas, to Miss Carol Jean Wolkins of Charleston, S. C., in Chicago, October 7.

DAVID SAMUEL GARNER, Roanoke, Va., to Miss Willye Mae Webb of Delray Beach, Fla., December 2.

IRVIN THOMAS BLANCHARD, Woodland, N. C., to Miss Lois Jean Bateman of Tarboro, November 17.

BEATY LEE BASS, Lenoir, N. C., to Miss Patsy Smith of Winston-Salem, in November.

IRVIN B. TRAPP to Miss Anne McGovern, both of Philadelphia, Miss., November 21.

CHARLES SWIFT JONES, New York, to Miss Frances Bird of Valdosta, Ga., December 18.

WALSH MCDERMOTT to Miss Marion Ann MacPhail, both of New York, November 11.

WALTER ELISHA HOOK to Miss Jeanne Patricia Diehl, both of Chicago, December 26.

JACOB D. MATIS to Miss Rosalie B. Metzger, both of Brooklyn, October 11.

Deaths

Warren La Verne Babcock ✠ Detroit; College of Physicians and Surgeons, Baltimore, 1893; formerly associate clinical professor of neurology and psychiatry at the Detroit College of Medicine and Surgery; secretary of the American Hospital Association from 1908 to 1910 and in 1911 president; president of the Michigan Hospital Association, 1919-1920 and 1934-1935; president of the Wayne County Medical Society, 1917-1918; was commissioned a first lieutenant and later a major and a lieutenant colonel in the medical corps of the U. S. Army during World War I; served as commanding officer of American Red Cross Hospital number 3 in Paris and later as commanding officer of Base Hospital number 6 in Bordeau; honorably discharged as a colonel in February 1919; was made an officer of the Legion of Honor of France in 1919; assistant physician at the Binghamton (N. Y.) State Hospital, 1894-1895, and the St. Lawrence State Hospital, Ogdensburg, from 1895 to 1902; chief surgeon of the New York State Soldiers' and Sailors' Home, Bath, N. Y., from 1902 to 1904; director of the Grace Hospital from 1904 to 1937 and treasurer and trustee since then; treasurer and trustee of the Michigan Hospital Service; on the editorial board of *Hospitals* and formerly on the editorial board of *Modern Hospital*; aged 69; died, December 27, at his winter home in St. Petersburg, Fla., of coronary thrombosis.

Thomas Wood Hastings, Kinderhook, N. Y.; Johns Hopkins University School of Medicine, Baltimore, 1898; instructor of clinical pathology at the Cornell University Medical College, New York, from 1901 to 1906 and professor from 1906 to 1918; substitute clinical pathologist, Presbyterian Hospital, New York, from 1902 to 1904; assistant visiting physician, Cornell Medical College Dispensary from 1901 to 1907; assistant visiting physician at the Bellevue Hospital, New York, from 1908 to 1917 and acting visiting physician from 1917 to 1921; member of the consulting staff of the St. Bartholomew's Clinic and Hospital, New York, 1920-1921; fellow of the American Association for the Advancement of Science; served in the Boer War in Africa, the Boxer Rebellion in China and during World War I; lieutenant in the medical reserve corps of the U. S. Army from 1910 to 1917, became a major in 1917 and retired with that rank in 1928; aged 69; died, December 5.

Elliott Gray Brackett ✠ Boston; Harvard Medical School, Boston, 1886; member of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; at one time assistant in orthopedics at his alma mater; served as a colonel and as a director of orthopedic surgery in the U. S. Army during World War I; one of the founders of the Industrial School for Crippled and Deformed Children; a trustee and the first president of the Boston School for Occupational Therapy; served as chief of the orthopedic service at the Massachusetts General Hospital and as assistant surgeon on the staff of the Children's Hospital; editor of the *Journal of Bone and Joint Surgery;* aged 82; died, December 29.

George Riley Anderson ✠ Brattleboro, Vt.; University of Vermont College of Medicine, Burlington, 1898; fellow of the American College of Surgeons; member of the New England Surgical Society; past president of the Vermont State Medical Society and of the Windham County Medical Society; veteran of the Spanish-American War; served as chief surgeon on the staff of the Brattleboro Memorial Hospital; consulting surgeon, Brattleboro Retreat, the Rockingham General Hospital, Bellows Falls and the Springfield (Vt.) Hospital; surgeon to the Boston and Maine Railroad; aged 67; died, December 19, in Winter Haven, Fla., of cerebral hemorrhage, arteriosclerosis and diabetes mellitus.

Henry Clay Lindersmith, Sherwood, Ohio; Barnes Medical College, St. Louis, 1894; member of the Ohio State Medical Association; formerly served as health officer of Defiance County; past president of the board of education of Sherwood and its first fire chief, serving for many years; at one time member of the board of U. S. Pension Examining Surgeons and local surgeon for the Baltimore and Ohio Railroad; aged 75; died, November 22, in the Mount Carmel Mercy Hospital, Detroit, of chronic myocarditis, hemorrhages and gastric ulcers of long duration.

Nagib Tannous Abdou, Utica, N. Y.; M.B., School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal in 1899 and M.D. in 1900; captain in the medical reserve corps of the U. S. Army not on active duty; aged 67; died, November 9, of coronary thrombosis.

Arne O. Arneson ✠ McVille, N. D.; George Washington University School of Medicine, Washington, D. C., 1911; served as vice president of the North Dakota State Medical Association; president of the Community Hospital; aged 63; died, December 11.

Bertha May Louise Lypps Bachelder, Pontiac, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; aged 65; died, December 14, of carcinoma.

Solomon Beck, New York; Columbia University College of Physicians and Surgeons, New York, 1910; formerly a pharmacist; aged 76; died, December 26.

Theodore Beck, Pleasant Hill, Ohio; Columbus Medical College, 1892; aged 79; died, December 15.

Gordian Edward Benes, St. Louis; National University of Arts and Sciences Medical Department, St. Louis, 1913; aged 57; died, December 9, of brain tumor.

Charles Albert Briggs ✠ Assonet, Mass.; Long Island College Hospital, Brooklyn, 1889; had been school physician in Freetown and Berkley for many years; aged 78; died, December 14, of cerebral hemorrhage.

Thomas Preston Cochran, Pittsburgh; Jefferson Medical College of Philadelphia, 1893; member of the Medical Society of the State of Pennsylvania; for many years president of the staff of St. Joseph's Hospital and Dispensary; formerly president of the Lyman Building and Loan Association and a director of the Hill Top Bank; aged 76; died, December 5.

John Elwood Cullum, Tulsa, Okla.; International Medical Missionary Institute, Chicago, 1900; Gate City Medical College, Texarkana, Ark., 1906; member of the Oklahoma State Medical Association; aged 83; died, December 6, of pneumonia and senility.

Arthur Ward Detrick ✠ New Carlisle, Ohio; Starling-Ohio Medical College, Columbus, 1908; for many years had been a member of the advisory board of the Clark County Health Board; aged 63; died, December 3, of cerebral hemorrhage.

Henry Trawick Donovan, Huntsville, Ala.; Louisiana State University Medical Center, New Orleans, 1934; formerly health officer of Shelby and Coffee counties; aged 35; died, December 7, in the Benevolent Society Hospital, Decatur, of injuries received in an automobile accident.

Leverette Saltanstall Early ✠ Petersburg, Va.; University College of Medicine, Richmond, 1898; served in the medical corps of the U. S. Army during World War I; local surgeon for the Norfolk and Western and Seaboard Air Line Railways; member of the chamber of commerce; aged 68; on the staff of the Petersburg Hospital, where he died, December 22, of multiple myeloma.

Joseph Benjamin Edwards, Swansea, S. C.; University of Maryland School of Medicine, Baltimore, 1911; member of the South Carolina Medical Association; served as medical examiner for the Selective Service System; during World War I served as a captain in the medical corps of the U. S. Army; won the Purple Heart and distinguished service citations; chairman of the board of trustees of the Swansea public schools for many years; aged 55; died, December 14, in the Veterans Administration Facility, Columbia, of heart disease.

George R. Ernst ✠ Wauwatosa, Wis.; Rush Medical College, Chicago, 1901; L.R.C.P., London and M.R.C.S., England, 1904; associate clinical professor of medicine at the Marquette University School of Medicine, Milwaukee; formerly superintendent of the tuberculosis division of the health department of Milwaukee; at one time superintendent of the Blue Mound Sanatorium; aged 73; died, December 3, of acute coronary thrombosis.

George W. Fiske, Rutland, Vt.; University of the South Medical Department, Sewanee, Tenn., 1901; aged 81; died, December 6.

John Edward Knight Flannagan ✠ Richmond, Va.; University of Virginia Department of Medicine, Charlottesville, 1925; formerly superintendent and medical director of the Roanoke City Tubercular Sanatorium, Roanoke; aged 43; died, December 2, in Wytheville of heart disease.

Louis Fuldner, Tryon, N. C.; Rush Medical College, Chicago, 1895; aged 69; died, December 11.

Thomas Monroe Garner, Somerset, Ky.; University of Louisville Medical Department, 1912; member of the Kentucky State Medical Association; past president of the Pulaski County Medical Society; aged 59; died, December 6, of organic valvular disease of the heart.

George John Geisler ✠ South Bend, Ind.; University and Bellevue Hospital Medical College, New York, 1915; served in France in the medical corps of the U. S. Army during World War I; major in the medical reserve corps, not in active duty; past president of St. Joseph County Medical Society; on the staffs of the Epworth and St. Joseph hospitals and the Children's Dispensary; aged 55; died, December 14, of coronary thrombosis and transverse myelitis.

Clarke Houston Gillespy ✠ Birmingham, Ala.; Tulane University of Louisiana School of Medicine, New Orleans, 1935; secretary-treasurer of the Jefferson County Medical Society; member of the Southeastern Surgical Congress; on the staffs of St. Vincent's, Hillman and Children's hospitals; aged 37; died, December 14, of metastatic adenocarcinoma.

William N. Goone ✠ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; served as a captain in the medical corps of the U. S. Army during World War I; aged 56; on the courtesy staff of the Lutheran Deaconess Hospital where he died, December 27, of coronary occlusion.

Ivan Bowman Hards, Denver; Grand Rapids (Mich.) Medical College, 1902; member of the New Mexico Medical Society; aged 64; died, December 14, of cardiovascular renal disease.

William A. Hoelscher, St. Louis; St. Louis College of Physicians and Surgeons, 1893; also a pharmacist; was vice president of the Cass Bank and Trust Company, where he had been a director for many years; aged 77; died, December 13, in Jacksonville, Fla.

George Michael Holley, Harrisburg, Pa.; Temple University School of Medicine, Philadelphia, 1930; aged 36; died, December 9, in the Good Samaritan Hospital, Pottsville, of amebic dysentery, hepatic abscess and diabetes mellitus.

Joseph Henry Keneally, Chicago; Harvard Medical School, Boston, 1900; aged 64; died suddenly, December 2.

Elmer O. Laughlin ✠ Paris, Ill.; Medical College of Ohio, Cincinnati, 1893; past president of the Aesculapian Society of the Wabash Valley; for many years surgeon for the Pennsylvania Railroad, a member of the library board and the city council; author of books and poetry; aged 75; died, December 14, of cerebral hemorrhage.

Herbert Edward Markwort, St. Louis; St. Louis College of Physicians and Surgeons, 1903; on the staffs of the Deaconess and St. Mary's hospitals; aged 65; died, December 11, of heart disease.

Joseph Chandler Marshall, Atlantic City, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; formerly on the staff of the Atlantic City Hospital; aged 69; died, December 20, of cerebral hemorrhage.

Henry Hamilton Mayne ✠ Lockport, N. Y.; University of Buffalo School of Medicine, 1892; pension examiner for the United States government from 1905 to 1912; served as a captain in the medical corps of the U. S. Army during World War I; coroner of Niagara County from 1895 to 1897 and again from 1900 to 1902; medical officer of the public schools of Lockport; aged 78; for many years on the staff of Lockport City Hospital, where he died, December 17, of a cerebral hemorrhage.

Cicero M. McCracken, Asheville, N. C. (licensed in North Carolina in 1896); member of the Medical Society of the State of North Carolina; was a member of the school board of Fairview; served on the county board of health; aged 74; died, December 8, of cardiorenal disease, hypertension and cerebral hemorrhage.

Thomas McLeod, Webster, Fla.; Atlanta (Ga.) Medical College, 1892; aged 78; died, December 11.

Henry P. Metcalf, Rushville, Ind. (licensed in Indiana in 1897); member of the Indiana State Medical Association; aged 86; died, December 15, of pulmonary embolus.

Robert Levis Mitchell ✠ Baltimore; University of Maryland School of Medicine, Baltimore, 1905; aged 61; on the staffs of the University Hospital and the Maryland General Hospital, where he died, December 13, of coronary thrombosis.

James Gordon Murfin, Portsmouth, Ohio; University of Pennsylvania Department of Medicine, Philadelphia, 1902; served as a captain in the medical corps of the U. S. Army during World War I; served on the staff of the Schirrman Hospital; aged 64; died, December 3, of edema of the lungs.

Prince Wellington Mynns, Brockton, Mass.; University of West Tennessee College of Medicine and Surgery, Memphis, 1916; aged 60; was found dead, December 4.

Elizabeth Naomi Newcomb, Carleton, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1916; formerly on the staff of the Woman's Hospital, Detroit; aged 57; died, December 7, in Detroit.

Arthur Thomas Piercy, Los Angeles; State University of Iowa College of Medicine, Iowa City, 1886; aged 85; died, December 3.

George Harris Richardson, Washington, D. C.; Howard University College of Medicine, Washington, 1890; formerly a lawyer; aged 88; died, December 2.

Howard Thomas Robinson ✠ Cumberland, Maryland; University of Maryland School of Medicine, Baltimore, 1904; member of the American Academy of Ophthalmology and Otolaryngology; on the courtesy staff of the Allegany Hospital of the Sisters of Charity; on the staff of the Memorial Hospital; aged 62; died suddenly, December 3, of coronary occlusion.

Herbert Ulysses Seabrook, Charleston, S. C.; University of West Tennessee College of Medicine and Surgery, Memphis, 1914; aged 56; died, November 17.

Albert Stein ✠ Thompsonville, Conn.; University of Maryland School of Medicine, Baltimore, 1917; served during World War I; on the visiting staff of the Wesson Memorial Hospital, Springfield, Mass.; aged 48; died, December 5, in the George F. Baker Clinic of the New England Deaconess Hospital, Boston, of uremia, acute hemorrhagic nephritis and pulmonary edema.

George A. Van Fradenburg, Manassa, Colo.; University of Denver Medical Department, 1898; aged 71; died, October 31, of carcinoma.

Richard Powers Wilkinson ✠ Philadelphia; Medico-Chirurgical College of Philadelphia, 1899; formerly treasurer of the Philadelphia County Medical Society; aged 70; died, December 2.

William Douglas Wirt, Washington, D. C.; Columbian University Medical Department, Washington, 1887; aged 80; died, December 13.

Leo Zon, Baltimore; University of Minnesota Medical School, Minneapolis, 1931; specialist certified by the American Board of Pathology, Inc.; diplomate of the National Board of Medical Examiners; passed assistant surgeon, U. S. Public Health Service reserve; aged 36; for many years research pathologist at the United States Marine Hospital, where he died, December 5, of meningococcic septicemia and cerebrospinal meningitis.

DIED WHILE IN MILITARY SERVICE

Maurice Marshall Berck ✠ New York; Cornell University Medical College, New York, 1928; diplomate of the National Board of Medical Examiners; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; on the staffs of the Mount Sinai and Gouverneur hospitals; captain in the medical corps, Army of the United States; entered active duty at the Army Medical Center, Washington, D. C., Nov. 24, 1942; aged 38; died, January 4, in the Central Dispensary and Emergency Hospital, Washington, of asphyxia, carbon monoxide, universal burns of the body and extremities, toxemia and shock, accidentally incurred when he probably fell asleep with a lighted cigaret in his hand and set his apartment on fire.

Lemuel Edward Day ✠ Chicago; Rush Medical College, Chicago, 1925; fellow of the American College of Surgeons; member of the attending staff, chairman, 1940-1941, section of obstetrics and gynecology at the Ravenswood Hospital, where he was president of the medical staff, 1933-1934; served as second lieutenant in the field artillery during World War I; major in the medical corps in the Army of the United States; began active duty June 14, 1942; in command of the Second Field Hospital, New Guinea, where he died, December 22, of heart disease, aged 46.

Jacob Walter, Chicago; University of Illinois College of Medicine, Chicago, 1939; a first lieutenant in the medical corps of the Army of the United States; was called to active service Feb. 5, 1941; stationed at the Milwaukee District United States Army Recruiting and Induction Service; aged 27; died, October 14, in the Veterans Administration Facility, Wood, Milwaukee, of lobar pneumonia.

Bureau of Investigation

SOME MISCELLANEOUS MEDICAL FRAUDS

A Variety of Schemes Debarred from the Mails

Fraud orders issued by the Post Office Department have frequently been the subject of extensive articles by the Bureau of Investigation in these pages of THE JOURNAL. Following are brief abstracts of some fraud orders not dealt with previously:

International Laboratories.—This is an outgrowth of, or a new name for, a Baltimore outfit that did an "obesity cure" mail order business under the name "The Bradford Laboratories." The fraud order that banned the Bradford concern from the mails was dealt with in a lengthy article in this department of THE JOURNAL, Jan. 4, 1941, pages 68-69. It was there shown that the Bradford outfit under one name or another had been in business over a period of more than forty years and at one time had claimed that its treatment was "composed of a combination of roots and herbs, no chemical preparations . . ." whereas it was represented still to be the original nostrum which chemical examination had shown to contain, among other ingredients, such minerals as baking soda and some bismuth salt, perhaps a subnitrate. The Post Office fraud order that closed the mails to this scheme was issued Dec. 1, 1939. Like many other swindles it did not actually go out of business but simply changed names and continued to operate as before, but under a new trade style, International Laboratories, Box 983, Baltimore, which had been contrived by E. L. Kincaid, the owner of the Bradford Laboratories. The actual address was 38 Hopkins Place, Baltimore, the same location from which the original enterprise had been conducted, but the new name and address were calculated to throw the Post Office off the scent. That agency, however, detected Kincaid's effort to dodge the original fraud order and on Sept. 29, 1941, issued a new one, debarring from the mails the name International Laboratories.

J. W. Dorman.—This person first came to the notice of the Bureau of Investigation when, on Oct. 15, 1934, trading as Dorman Chemical Company, Concord, N. C., he was fined $100 and placed on probation for eighteen months after pleading guilty to violating the Pure Food and Drugs Act by shipping his "J-W-D Blood Purifier" and undesignated pills and capsules in interstate commerce under the fraudulent label representations that the complete treatment was a blood purifier and general reconstructive tonic, as well as a cure for pellagra, kidney and heart disorders, ulcerated stomach, high blood pressure, gallstone trouble, skin diseases and some other conditions. This case, designated by the government as Notice of Judgment 24515, issued in March 1936, was abstracted in THE JOURNAL, Sept. 25, 1937. Dorman, using not only his name but also the title "The Medicine Man" also sold his treatment by mail, playing it up chiefly as a treatment for pellagra. In his circulars he claimed that he had once suffered from this disease in its worst form and that a hospital which treated him for it discharged him as an incurable patient. Thereupon, if one could believe him, "he sought to relieve himself by experimenting with different herbs. He discovered a combination by which he was completely relieved. Since that time he has been making and selling this medicine to relieve other sufferers. Thousands have been completely relieved and there is no case recorded that we know which has failed to be relieved when the medicine has been taken according to directions." Testimonials, the usual stock in trade of the "patent medicine" exploiter, also were played up, but when asked to produce the alleged originals of these he was unable to do so. Analysis by government chemists revealed that one part of the treatment, "J. W. D." consisted essentially of tincture of digitalis, Fowler's solution of arsenic, salicylic acid, coloring matter and water. The accompanying blue tablets contained copaiba, cubebs, methylene blue, santal and kava kava; the white tablets were a mixture of aloes, podophyllum, colocynth, scammony, gamboge and about 0.8 grain per tablet of calomel; the ointment contained sulfur, petrolatum, hydrous wool fat, a hot principle, a phenolic principle and a salicylate. As evidence of the scientific character of this treatment it is interesting to note that the Post Office investigation divulged that Dorman could neither read nor write and that the clerical details of his business had to be performed by his wife. When cited by the Post Office to appear at a hearing held on Jan. 13, 1937, and show cause why a fraud order should not be issued against his enterprise, Dorman sent his attorney instead. Since the latter was unable to controvert the evidence presented by the expert medical witness for the government to the effect that Dorman's nostrums were wholly without value for pellagra, his business was debarred from the mails by a fraud order issued Jan. 25, 1937, against the names J. W. Dorman, "The Medicine Man," and Dorman Chemical Company. Some time thereafter, according to a later Post Office investigation, Dorman moved from Concord to Pineville, N. C., where he continued to operate his scheme despite the original fraud order. In response to one inquiry he claimed that his present pellagra treatment was the same as the one he formerly had sold from Concord. When asked whether it would cure pellagra, he sent the treatment through the mails for that purpose, designating it as "J. W. D. (An Alterative)," "Dorman's Diuretic Tablets" and "J. W. D. Laxative Tablets," and asking $3.50 for the combination. A government chemist who analyzed these nostrums reported that the first named was a reddish-pink liquid containing total medicinal matter amounting to 0.04 grain per teaspoon and containing in each teaspoon 0.009 grain of arsenic trioxide, 0.02 grain of salicylic acid and a trace of wintergreen. The "diuretic tablets" were found to contain copaiba, cubeb, methylene blue, santal oil and kava kava, and the "laxative tablets" consisted of rhubarb, colocynth compound and about 8/10 of a grain of calomel. When Dorman was notified by the Post Office to show cause why a second fraud order should not be issued against him he neither put in an appearance nor sent anyone to represent him, his sole defense being a written answer to the charges. An expert medical witness, familiar with pellagra, testified for the government that this is a vitamin deficiency disease manifested by many symptoms and that the present recognized treatment for it is the administration of nicotinic acid in large doses, together with an abundance of other vitamins, such as thiamine (B_1) and riboflavin (B_2) as well as proper diet. Since it was shown that Dorman's group of nostrums would not cure or alleviate pellagra and that, in fact, the use of a laxative such as his treatment included might set up an intractable diarrhea endangering the very life of the sufferer, it was declared to be a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises, and an evasion of the fraud order of Jan. 25, 1937. A supplemental fraud order, accordingly, was issued on Oct. 28, 1942, against J. W. Dorman of Pineville, N. C.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 15-16, 1943. Sec., Council on Medical Education and Hospitals, Dr. H. G. Weiskotten, 535 North Dearborn Street, Chicago.

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Jan. 23, page 281.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, March 1-3. Exec. Sec., Mr. Everett S. Elwood, 225 S. Fifteenth St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral. Part II.* New York, May 15-16. San Francisco, May 22. Chicago, June 6-7. Final Date for filing application is 90 days prior to date of examination. Sec., Dr. P. M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, Feb. 15-16. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 13. Candidates in military service may take Part I at their place of duty. *Oral. Part II.* Pittsburgh, May 19-25. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral. All Groups. Parts I and II.* March 1. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* New York, May or June. Final date for filing application is March 1. Sec., Dr. Dean M. Lierle, 1500 Medical Arts Bldg., Omaha, Neb.

AMERICAN BOARD OF PEDIATRICS: Starting July 1, 1943, Group I will be abolished. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY & NEUROLOGY: Various centers, April or May. Final date for filing application is March 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 12-14. Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis.

Montana October Report

The Montana State Board of Medical Examiners reports the written examination for medical licensure held at Helena, Oct. 6-7, 1942. The examination covered 10 subjects and included 50 questions. An average of 75 per cent was required to pass. Eight candidates were examined, 7 of whom passed and 1 failed. Six physicians were licensed to practice medicine by reciprocity and 3 physicians so licensed on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

PASSED

School	Year Grad.	Number Passed
University of Minnesota Medical School	(1935)	1
Creighton University School of Medicine	(1942, 2)	2
Ohio State University College of Medicine	(1942)	1
Medical Department of Grant University	(1897)	1
Marquette University School of Medicine	(1942)	1
Université de Lausanne Faculté de Médecine	(1936)	1

FAILED

School	Year Grad.	Number Failed
Universität Zürich Medizinische Fakultät	(1940)	1

LICENSED BY RECIPROCITY

School	Year Grad.	Reciprocity with
College of Medical Evangelists	(1930)	California
Rush Medical College	(1937)	Maryland
University of Minnesota Medical School	(1926), (1942)	Minnesota

University of Manitoba Faculty of Medicine	(1930)	N. Dakota
University of Toronto Faculty of Medicine	(1895)	Michigan

LICENSED BY ENDORSEMENT

School	Year Grad.
Johns Hopkins University School of Medicine	(1921)
Tufts College Medical School	(1939)
Universidad Central de Espana Facultad de Medecina, Madrid	(1933)

Maryland June Report

The Board of Medical Examiners of Maryland (Homeopathic) reports the written examination for medical licensure held at Baltimore, June 16-17, 1942. The examination covered 9 subjects and included 70 questions. An average of 75 per cent was required to pass. Four candidates were examined, all of whom passed. The following schools were represented:

PASSED

School	Year Grad.	Number Passed
Hahnemann Medical College and Hospital of Philadelphia	(1941, 3), (1942)	4

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Right to Require Alleged Incompetent in Guardianship Proceedings to Submit to Mental Examination.—Redfield applied to the superior court, King County, Washington, for the appointment of a guardian of the person and estate of his sister, alleging that she was incompetent mentally and physically to care for herself or her estate. Subsequently the trial court ordered three psychiatrists, named by Redfield, to examine the alleged incompetent to enable them to testify later as to her physical and mental condition at the hearing on the petition for the appointment of a guardian. The state, then, on the relation of the alleged incompetent, brought certiorari to the Supreme Court of Washington to review the propriety of the trial court's order.

While Redfield cited no court decision which specifically held that in a guardianship proceeding the trial court may, before a hearing, direct that the alleged incompetent submit to an examination by physicians named by the court to conduct such an examination, he contended that such power is included in the general inherent authority of the court to conduct guardianship proceedings and to take such steps as may be deemed advisable in order that a full and complete hearing may be had. Apparently as authority for an order such as was under question, he relied on *Lane* v. *Spokane Falls & Northern R. Co.*, 21 Wash. 119, 57 P. 367, in which the Supreme Court of Washington held that the trial court possessed inherent power to require a plaintiff in a tort action for personal injuries to submit to a pretrial examination by medical experts appointed by the court for the purpose of ascertaining the nature, character and extent of the plaintiff's injuries. The Supreme Court, however, distinguished that case from the facts here involved. Obviously, said the court, when a person voluntarily brings an action for the recovery of damages on account of personal injuries alleged to have been suffered, the court should have the power to direct that, prior to the trial, the plaintiff submit to a physical examination. There is no statute in this state authorizing such action in an adversary proceeding for the appointment of a guardian of an alleged incompetent nor would such a right seem to be vested in the court at common law. The right of a court to order a party to submit to a physical examination was recognized at common law in certain classes of actions, such as proceedings for divorce, in cases in which it was desired to make proof of heirship and in criminal prosecutions for mayhem. The right of the court in Washington is somewhat broader than at common law because of a Washington statute (Rem. Rev. Stat., sec. 6930) which provides that when it is charged under oath that a person, by reason of insanity, is unsafe to be at large, the court can require the alleged incompetent to submit to examination by two reputable physicians. But this procedure applies only under and is limited to the circumstances mentioned.

The authority assumed by the trial court, continued the Supreme Court, in ordering the alleged incompetent to submit to an examination to be conducted by physicians designated by the person seeking the appointment of a guardian trenches to a great extent on the liberty of the individual. One in the alleged incompetent's situation is not a voluntary participant in such a proceeding as this. The proceeding is adverse to her. It may be assumed that, in the great majority of cases, no petition alleging incompetency would be filed unless at least some ground existed for such a charge. Assuming, then, that the alleged incompetent is physically or mentally ill, the charge of incompetency itself would naturally have a bad effect on the person and tend to aggravate any unfortunate existing condition. If, in addition to the charge, the alleged incompetent must submit to the ordeal necessarily involved in a lengthy physical and mental examination by three physicians known to have been chosen by the adverse party, the effect would probably be very bad and might be serious. There would be no way of terminating the examination until the examining physicians chose to end it, and its undue extension might well be most unfair and harmful to the subject. Neither would there be any control of the questions that the examiners might ask, and, even though the subject might be represented and advised by counsel, the mere persistent asking of improper questions might well irritate the person examined and produce unfortunate results.

A petition for the appointment of a guardian on the ground of mental incompetence, continued the court, may be filed against any person at any time. If the procedure embodied in the order now before this court for review may be established, it might be used improperly and for some ulterior purpose entirely disconnected from any question of guardianship. In the absence of any controlling authority, such as the presence of the judge, much harm might result. Certainly no such step should be taken unless the judicial authority to make the order clearly appears and some very real emergency should be shown to exist. The ordeal of appearing in court, or even knowing that such a proceeding has been filed, is considerable, but those consequences cannot be avoided. In open court the alleged incompetent has the benefit of judicial protection. If, in the course of the hearing before the court on the application for appointment of a guardian, the court feels that the evidence produced is inadequate, or for any reason unsatisfactory, and for its own information desires further testimony, a different situation might arise, concerning which we here express no opinion. The effect of holding the procedure followed in entering the order under review proper would seem to encourage the filing of a petition for the appointment of a guardian since a petitioner could use physicians of his own selection by way of an exploring expedition to see what they could discover in examining an alleged incompetent. In this case the order provided that the three physicians named should make only one examination of the alleged incompetent and that the time should suit her convenience, but even with that restriction the accomplishment of the order would require that the alleged incompetent undergo a very trying ordeal, which might have to her injurious consequences.

The order in question, the court accordingly held, was entered without warrant of law and infringed the alleged incompetent's lawful rights to personal peace and security. The order requiring the alleged incompetent to submit to examination by physicians designated by her brother was reversed.—*State ex rel. Nelson v. Superior Court of King County, 131 P. (2d) 144 (Wash., 1942).*

Society Proceedings

COMING MEETINGS

Annual Congress on Medical Education and Licensure, Chicago, Feb. 15-16. Dr. H. G. Weiskotten, 535 North Dearborn St., Secretary.

American Society of Anesthetists, New York, Feb. 4. Dr. Paul M. Wood, 745 Fifth Avenue, New York, Secretary.

Conference of State and Provincial Health Authorities of North America, Washington, D. C., March 22-25. Dr. A. J. Chesley, 469 State Office Bldg., St. Paul, Secretary.

Western Section, American Laryngological, Rhinological and Otological Society, Portland, Ore., Jan. 31. Dr. Irving M. Lupton, 1020 S.W. Taylor St., Portland, Ore., Chairman.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

24:579-718 (Nov.) 1942

Interrelationship of Disease of Coronary Arteries and Gallbladder. H. R. Miller, New York.—p. 579.
Auricular Flutter Associated with Bizarre QRST Complexes. J. S. Butterworth and C. A. Poindexter, New York.—p. 588.
Influence of Posture on Electrocardiogram. H. S. Mayerson and W. D. Davis Jr., New Orleans.—p. 593.
Auricular Complex in Coronary Thrombosis. N. Bloom and D. Gilbert, Richmond, Va.—p. 602.
*Weltmann Serocoagulation Band in Myocardial Infarction. J. H. Delaney, Columbia, Mo., and J. W. Keyes, Detroit.—p. 607.
*Diagnostic Value of Electrocardiogram Based on Analysis of 149 Autopsy Cases. L. N. Katz, A. M. Goldman, R. Langendorf, L. G. Kaplan and S. T. Killian, Chicago.—p. 627.
Dissecting Aneurysm of Aorta. N. Flaxman, Chicago.—p. 654.
Electrocardiographic Changes Following Electrically Induced Convulsions. E. M. Kline and J. L. Fetterman, Cleveland.—p. 665.
Studies on Coronary Occlusion: III. Effect of Digitalis on RST Segment of Electrocardiogram After Coronary Ligation. M. G. Mulinos and A. Leslie, New York.—p. 671.
Id.: IV. Vasodilators and Coronary Circulation: Experimental Observations. A. Leslie and M. G. Mulinos, New York.—p. 679.

Weltmann Serocoagulation Band.—The interest of Delaney and Keyes in the application of the Weltmann serocoagulation test in coronary artery occlusion was aroused by the parallelism between this test and the sedimentation rate and leukocyte count in other conditions characterized by tissue necrosis. The coagulation band of the Weltmann serocoagulation test was considerably shortened in 24 cases of coronary artery occlusion. The coagulation band became progressively shortened during the early acute stages of infarction, beginning on the second or the third day, and reached its minimum by the fifth to the seventh day. This "shift to the left" afforded some index of the extent of myocardial necrosis. An abrupt, extreme or persistent left shift would indicate either a large infarction or slow healing and therefore a more serious prognosis. Conversely, a coagulation band which is only moderately shortened or promptly returns to normal was associated with satisfactory healing and a good prognosis. As repair proceeds by fibrosis, the coagulation band lengthens again to normal. Large areas of fibrosis, old or recent, result in a shift to the right, beyond normal. The Weltmann reaction may serve as a manifestation of the actual pathologic course of the disease. In coronary artery insufficiency, which produces myocardial ischemia without actual infarction, the coagulation band is unchanged. Therefore the Weltmann test is useful in differentiating between the two conditions. The conditions (pregnancy, the ingestion of food and destructive changes in the body) that cause variations in the sedimentation rate are not observed to do so in the Weltmann test, which more closely reflects the true nature of the pathologic change and the clinical course of the patient. There was a close parallelism between the Weltmann coagulation band and the nonfilament count. The two complicating factors which must be considered in interpreting the coagulation band are the presence of old or new fibrotic processes of cardiac or extracardiac origin and myocardial insufficiency. The data obtained from a frequent charting of the Weltmann serocoagulation reaction are superior to those obtained with any other single procedure.

Diagnostic Value of Electrocardiogram.—The electrocardiographic and the necropsy observations of 149 consecutive cases were compared by Katz and his co-workers. In cases of combined hypertrophy of the right and left ventricles the electrocardiogram usually reflected only the predominant ventricular strain. Right ventricular preponderance was more often correctly diagnosed and less often overlooked than left ventricular preponderance. However, decided hypertrophy, especially if both ventricles are involved, may be present without electrocardiographic evidence of ventricular strain. Old healed infarction of the anterior wall may be indistinguishable from left ventricular hypertrophy without myocardial infarction. Conversely, left ventricular hypertrophy may give rise to an electrocardiographic pattern suggestive of recent infarction of the anterior wall. The electrocardiographic pattern of congenital heart disease was diagnostic. The patterns associated with recent myocardial infarction were significant, although errors did occur, but errors were less likely when chest leads and serial curves were obtained. Old healed myocardial infarction, coronary sclerosis and myocardial fibrosis commonly failed to produce any characteristic electrocardiographic pattern. The electrocardiographic localization of myocardial infarction was correct in all but 1 case of old healed infarction. In the 2 cases of infarction of the lateral wall there were anterior wall patterns in the limb leads. Recent diffuse pericarditis was recognized in the electrocardiogram in the presence of associated masking conditions. The patterns of acute cor pulmonale were diagnostic, but extensive massive pulmonary embolism may occur without these patterns. Chronic cor pulmonale may produce a diagnostic pattern. The mitral P wave pattern is indicative of left auricular involvement, and, in the present series, it constituted electrocardiographic evidence of rheumatic heart disease.

American Journal of Physiology, Baltimore

137:641-798 (Nov.) 1942. **Partial Index**

Effects of Heightened Negative Pressure in Chest, Together with Further Experiments on Anoxia in Increasing Flow of Lung Lymph. Madeleine F. Warren, Delores K. Peterson and C. K. Drinker, Boston.—p. 641.
Volume of Air Moved by Artificial Respiration in Anesthetized Men. D. R. Hooker, W. B. Kouwenhoven and J. A. York, Baltimore.—p. 649.
Role of Adrenal Cortex in Preventing Hypoglycemic Convulsions. V. Arnett, M. Kessler and E. Gellhorn, Chicago.—p. 653.
Control of Clonic Responses of Cerebral Cortex. A. Rosenblueth, D. D. Bond and W. B. Cannon, Boston.—p. 681.
Effect of Peripheral Vasodilatation on Vasoconstriction: Determinations Made on Basis of Blood Pressure of Normal Subjects. Grace M. Roth and C. Sheard, Rochester, Minn.—p. 695.
Production of Experimental Polycythemia by Daily Administration of Epinephrine or Posterior Pituitary Solution. J. E. Davis, Little Rock, Ark.—p. 699.
Distribution of Sucrose in Body Fluids Following Intravenous Injections. R. S. Hubbard and R. K. Anderson, Buffalo.—p. 722.
*Effects of Diet Deficient in Vitamin B Complex on Sedentary Men. F. Egaña, R. E. Johnson, R. Bloomfield, L. Broncha, A. P. Meiklejohn, J. Whittenberger, R. C. Darling, C. Heath, A. Graybiel and F. Consolazio, Boston.—p. 731.
Acid Base Equilibrium of Blood in Exercise. E. S. Turrell and S. Robinson, Bloomington, Ind.—p. 742.
Relationship Between Monochromatic Light and Pupil Diameter: Low Intensity Visibility Curve as Measured by Pupillary Measurements. I. H. Wagman and J. E. Gullberg, Berkeley, Calif.—p. 769.
Effect of Injured Area on Electrical Field of Heart Based on Experiments with Models. L. N. Katz, K. Jochim and A. Goldman, Chicago.—p. 779.

Vitamin B Complex Deficiency in Sedentary Men.—Egaña and his collaborators show that a diet grossly deficient in the vitamin B complex causes subjects to become deficient (as determined by urinary excretion) within three or four weeks, that there is measurable physical deterioration in this time and that brewers' yeast is a complete and adequate supplement to the deficient diet. The subjects used were 7 healthy physicians. The symptoms of physical deterioration were mild and vague, the most constant being easy fatigue, loss of ambition and loss of efficiency in daily work. Physical fitness for exhausting exercise and, particularly, recuperation between repeated periods of exhausting exercise were moderately deteriorated. The changes were reversed by adding brewers' yeast to the diet. All other metabolic measurements showed slight or no abnormal changes. These measurements were oxygen consumption, carbon dioxide excretion, blood lactate, blood pyruvate, blood sugar, urine lactate and urine pyruvate. Cardiovascular changes were inconstant; there never was a tachycardia on exertion. On the contrary, abnormally slow heart rates in moderate exercise and in exhausting exercise were the rule. Blood pressure did not change. The electrocardiogram of only 1 subject showed significant changes.

Annals of Surgery, Philadelphia

116:641-800 (Nov.) 1942

Practical Concept for Treatment of Major and Minor Burns: Importance of Timing Therein. F. B. Gurd, D. Ackman, J. W. Gerrie and J. E. Pritchard, Montreal, Canada.—p. 641.
*Study of "Shock Delaying" Action of Barbiturates; with Consideration of Failure of Oxygen Rich Atmospheres to Delay Onset of Experimental Shock During Anesthesia. H. K. Beecher, Jane D. McCarrell and E. I. Evans, Boston.—p. 658.
Chest Injuries. F. S. Dolley and L. A. Brewer 3d, Los Angeles. —p. 668.
Pilonidal Cysts and Sinuses: Method of Wound Closure: Review of 230 Cases. W. F. MacFee, New York.—p. 687.
Successful Closure of Arteriovenous Aneurysm Involving Left Innominate Vein and Left Common Carotid Artery. H. Tarnower, B. Lattin, Scarsdale, N. Y., and G. C. Adie, New Rochelle, N. Y.—p. 700.
Complicated Case of Aneurysm Involving Iliac and Femoral Arteries. L. N. Atlas, Cleveland.—p. 708.
Comparison of Results of Roentgen Rays, Sulfanilamide and Serum Therapy in Experimental Gas Gangrene in Pigeon. W. H. Erb and P. J. Hodes, Philadelphia.—p. 713.
*Noninfective Gangrene Following Fractures of Lower Leg. C. G. Child 3d, New York.—p. 721.
Recurrent Ulceration Following Subtotal Gastrectomy in Treatment of Gastroduodenal Ulcer. S. Mage, New York.—p. 729.
*Primary Carcinoma of Duodenum. L. Berger and H. Koppelman, Brooklyn.—p. 738.
Solitary Nonparasitic Cyst of Liver. H. S. Munroe Jr., Charlotte, N. C. —p. 751.
Studies on Use of Metals in Surgery: II. Experiments on Use of Ticonium in Cranial Repair. E. Campbell, A. Meirowsky and V. Tompkins, Albany, N. Y.—p. 763.
Use of Lamp to Warm Moist Compresses. H. E. Pearse, Rochester, N. Y.—p. 776.
Anatomic Approach to Pulmonary Resection. E. M. Kent and B. Blades, St. Louis.—p. 782.

"Shock Delaying" Action of Barbiturates.—According to Beecher and his co-workers, the observation of Seeley, Essex and Mann that shock produced in dogs by exposure and manipulation of the intestine is slower to appear when barbiturate (sodium amytal) anesthesia than when ether anesthesia is used has been confirmed. There was no significant delay in the onset of shock produced by hemorrhage when barbiturate (sodium amytal) or ether anesthesia was used. This observation indicates that the barbiturates as compared with ether anesthesia are not useful in delaying all types of shock. The barbiturates appear to delay shock in comparison with ether only when the trauma is associated with loss of plasma from wound surfaces. The recommendation that barbiturates be administered to all wounded men if shock is anticipated involves two major assumptions, both of which, on the basis of the available information, are untenable: First, the recommendation that barbiturates be given all seriously wounded men assumes that the barbiturates will be of value in all types of shock, which is not the case. The assumption that such administration of barbiturates will not be dangerous is contradicted by abundant evidence. Second, direct application as a shock delaying or preventive requires the assumption that comparison of the barbiturate data with the ether data is the same as a comparison of barbiturate data with a condition of no anesthesia. No data are available to indicate that the onset of shock is slower under barbiturates than in the unanesthetized subjects. In experiments the administration of approximately 100 per cent oxygen did not significantly delay, in comparison with room air, shock due to bleeding under a barbiturate or ether anesthesia.

Gangrene Following Fractures.—Child reports the fifteenth case of noninfective gangrene following fracture of the lower leg. In his patient, who was 23, a careful analysis of the complication reveals two features of significance: 1. The nerve supply of the lower leg and foot, which was intact on admission, failed during the next two or three days. 2. The blood supply of the foot, which also was normal on admission, showed early signs of embarrassment, followed, however, by ultimate survival of the member. With these facts in mind it is possible to reconstruct the course of events that led to the complication. As a result of the severe crushing nature of the injury the anterior tibial artery probably was torn sufficiently to damage its intima, and a thrombus began to form at the site of the injury. During the next few days the thrombus became so large that it occluded the lumen of this vessel. Dependent on the progressive nature of this lesion were the clinical phenomena, namely the intact nerve and blood supply on admission, their eventual failure as the integrity of the blood supply became compromised and finally gangrene and complete loss of sensation. The ultimate viability of the foot may in all probability be ascribed to the rich collateral circulation about the ankle joint and between the distal branches of the anterior and posterior tibial arteries in the foot, but although this was abundant it was inadequate to supply in retrograde fashion the proximal portion of the anterior tibial arteries. To establish the validity of these assumptions the 14 cases of this complication appearing in the literature from 1850 to the present time are reviewed. Analysis reveals that the average age for the 15 was 26 years, and therefore degenerative diseases of the arterial wall as predisposing factors can be discounted. With two exceptions the fractures were extensive and involved both bones of the lower leg. The sites of fracture were about evenly distributed between the upper, middle and lower thirds of the lower leg; some were compound, some oblique, some transverse and many were comminuted. Apparently no particular site or type of fracture was especially predisposing. The gangrene in 9 involved the lower leg and foot, in 5 the foot alone and in 1 only the lateral muscles of the calf. The condition in all but 2 required that amputation be carried out. The site of the occlusive process in the other 13 was located; in 4 it was the popliteal, in 8 the anterior and posterior and in 1 the posterior tibial arteries. The complication in all probability does not appear to be related to the method of immobilization employed. Of the 2 patients on whom amputation was not done, the 1 who refused amputation was left with a useless leg and 1, the author's patient, is left with a foot which functions only partially even when supplemented by a brace. There were no deaths.

Carcinoma of Duodenum.—A proved case of primary carcinoma of the infrapapillary portion of the duodenum is presented by Berger and Koppelman, who discuss the roentgen, operative and necropsy observations from a clinical point of view. In the literature on all types of primary duodenal carcinoma 386 proved cases are reported to date, of which 19.9 per cent were suprapapillary, 65 per cent peripapillary and 15 per cent infrapapillary. Earlier diagnosis depends on the clinician's awareness that the diagnosis of duodenal carcinoma is possible though rare (from 0.03 to 0.003 per cent of all necropsies). Roentgen examination is especially helpful if the lesion is looked for consciously. While the results of radical surgery in duodenal carcinoma have been discouraging (5.2 per cent five year cures), with earlier diagnosis and with the present improved methods of preoperative and postoperative care the prospect for the future looks brighter, since a rational surgical technic is available for each type of case and since metastasis at the time of exploration is low.

Archives of Pathology, Chicago

34:937-1096 (Dec.) 1942

Experimental Cholesterol Atheromatosis in Omnivorous Animal, the Chick. D. V. Dauber and L. N. Katz, Chicago.—p. 937.
Localized Pleural Mesothelioma: Investigation of Its Characteristics and Histogenesis by Method of Tissue Culture. A. P. Stout and Margaret R. Murray, New York.—p. 951.
Heretofore Unrecognized Mechanical Principle Effective in Aortic Sclerosis. J. Krafka Jr., Augusta, Ga.—p. 965.
Elastic Tissue: II. Study of Elasticity and Tensile Strength of Elastic Tissue Isolated from Human Aorta. G. M. Hass, New York.—p. 971.
Atrophy, Degeneration and Metaplasia in Denervated Skeletal Muscle. R. Altschul, Saskatoon, Sask., Canada.—p. 982.
Arteriosclerosis Obliterans: Study of Lesion in Occluding Peripheral Sclerosis with Note on Mönckeberg's Sclerosis. S. W. Sappington and H. R. Fisher, Philadelphia.—p. 989.
Heterotopic Brain Tissue in Lungs of Two Anencephalic Monsters. Edith L. Potter and R. L. Young, Chicago.—p. 1009.
Transposition of Aorta and Pulmonary Artery: Embryologic Study of Its Cause. J. L. Bremer, Boston.—p. 1016.
Adrenal Cortex in Essential Hypertension. W. S. Dempsey, Montreal, Canada.—p. 1031.
Production of Cirrhosis of Liver in Rats by Feeding Low Protein, High Fat Diets. H. Blumberg, Baltimore, and H. G. Grady, Darby, Pa. —p. 1035.
Parathyroid Gland in Infancy. E. Kaplan, Boston.—p. 1042.
Equine Encephalomyelitis (Western) in Man: Histologic and Anatomic Study. J. H. Peers, Bethesda, Md.—p. 1050.
Effects of Radiation on Normal Tissues: IV. Effects of Radiation on Cardiovascular System. S. Warren, Boston.—p. 1070.
Id.: VII. Effects of Radiation on Urinary System. S. Warren, Boston.—p. 1079.

Archives of Physical Therapy, Chicago

23:641-704 (Nov.) 1942

Poliomyelitis and Public Health. D. W. Gudakunst, New York.—p. 645.
Treatment of Infantile Paralysis in Acute Stage. J. A. Toomey, Cleveland.—p. 650.
*Basis for Transitions in Physical Treatment of Poliomyelitis. Jessie Wright, Pittsburgh.—p. 662.
*Kenny Treatment for Infantile Paralysis. M. E. Knapp, Minneapolis. —p. 668.

Transitions in Physical Treatment of Poliomyelitis.—A comparison of observations in cases of poliomyelitis treated by early immobilization and by the Kenny method suggests, Wright states, that early judicious use of fomentations and physiologic movements as pain and tenderness subside tend to absorb products of effusion, relieve muscular spasm and limit scar tissue which may ensnare normal neuromuscular units. Thus residual paralysis may be confined to the neuromuscular units which have been primarily and permanently injured by the virus. The rationale of making a transition from the early rigid rest and splinting to starting physical treatment immediately after diagnosis is confirmed. Wright believes that Miss Kenny's most important contribution to the treatment of infantile paralysis is in arousing the medical profession to use her method early in the acute stage of the disease and thus prevent much impaired circulation, fibrosis, loss of muscle sense and restriction of joint action so common when early treatment consisted of rigid rest and extensive splinting. Much of the residual damage to patients so treated was probably due to muscular spasm that was never relieved by immobilization.

Kenny Treatment for Infantile Paralysis.—Knapp discusses muscle spasm, mental alienation and incoordination, the three basic ideas which differentiate the Kenny conception of the symptomatology of infantile paralysis. Paralysis is common to the two concepts. Muscle spasm is one of the basic symptoms—it is an involuntary and uncontrollable shortening of muscle fibers. This spasm is not to be confused with the spasticity of an upper motor neuron lesion which will relax under steady tension. Some of the possible local mechanisms responsible for the spasm are inflammatory or toxic changes and circulatory changes resulting in localized anoxia. However, the local condition may also be due to changes in the central nervous system. The so-called irritative cord lesions may account for spasm. As denervated muscle is hypersensitive to acetylcholine, local spasm could be caused by a pathologic change in the cord. It is probable that fibrosis and contractures may be due to anoxia caused by spasm. It also seems reasonable that permanent pathologic changes may thus be produced by the spasm itself, even without extensive loss of motor cells. Consideration of these factors lends weight to the argument that muscle spasm should be treated and relieved as soon as the diagnosis has been made and that splinting, which favors spasm, should be avoided. Mental alienation is probably a physiologic block in conduction as contrasted with an anatomic block caused by destruction of anterior horn cells. Under this term may be included temporary paralysis produced by nonlethal damage to the nerve cells which recover spontaneously after the infection has subsided. Kabat has suggested the term "reversible paralysis" instead of "mental alienation." The conception of "mental alienation" is a valuable one if for no other reason than to suggest a possible effective treatment. Incoordination means that, because of disturbances in the normal motor patterns as a result of paralysis, alienation or spasm, new motor patterns are developed which must become normal before normal action can occur. Evidence for the support of this idea is supplied by numerous patients who have been treated by the Kenny method months or years after unsuccessful treatment by conventional methods and who have been able to walk without support or have been able to use parts which previously were useless. The increase in useful function is due not to increase in power but to increase in coordination and decrease in limitation of motion from muscle shortening, so that the efficiency of the muscle is greater.

Bulletin of Johns Hopkins Hospital, Baltimore

71:253-314 (Nov.) 1942

Factors Influencing Level of Vitamin A in Blood of Rats. H. W. Josephs, Baltimore.—p. 253.
Studies in Vitamin A: Influence of Vitamin A on Serum Lipids of Normal and Deficient Rats. H. W. Josephs, Baltimore.—p. 265.
Evaluation of Progesterone Therapy in Treatment of Endometrial Hyperplasia. G. E. S. Jones and R. W. Te Linde, Baltimore.—p. 282.
Spirochetal Survival in Frozen Plasma. M. M. Ravitch and J. W. Chambers, Baltimore.—p. 299.
*Sulfonamide Film for Use as Surgical Dressing: Preliminary Report. K. L. Pickrell, Baltimore.—p. 304.

Sulfonamide Film as Surgical Dressing.—While studying various drying agents and plastic substances it occurred to Pickrell that a preformed sulfonamide film might serve a useful purpose in surgery. The film is made in the following manner: An emulsion is prepared containing 3 per cent of sulfadiazine or sulfanilamide, 2.5 per cent of methyl cellulose, 3 per cent of triethanolamine and 0.5 per cent of sorbitol with 50 per cent alcohol or acetone added to make 100 cc. The resulting emulsion is sprayed with a pressure gun or paint spray on a smooth horizontal glass surface. This is allowed to dry; if acetone is used drying is extremely rapid, but if 50 per cent alcohol is used several hours at 75 C. are required before the film can be removed in a single sheet. The films are stable and can be sterilized by dry heat. Composition studies reveal that the film ordinarily contains 35 to 50 per cent of the sulfonamide compound. When a segment of the film is placed beneath the skin of a rabbit the sulfonamide can be detected in the blood within several hours. At the end of twenty-four hours, disintegration of the film is almost complete. The author has used these sulfonamide films for 50 patients with burns in whom a surgical detergent was used to clean the burned surface and the surrounding skin if it was grossly contaminated. The area was then washed with saline solution, sulfadiazine or azochloramid solution. While the surface was still moist the sulfonamide film was placed to overlap the burned surface. A smooth, firm pressure dressing of gauze was then applied. This film remains in place for three to five days, at which time epithelization will be taking place in second degree burns. Since the film is translucent, the injured area may be inspected without removing it. In third degree burns and in exudative lesions the film may be renewed as desired. The film has also been used to cover recent incisions, lacerations and abrasions, to prepare granulating areas for grafting, to cover the recipient and donor graft areas at the time of grafting, to cover abraded and ulcerated areas and as a framework to hasten closure and regeneration of perforated eardrums. If low concentrations of the sulfonamides were used in the films, infection was likely. Sulfadiazine films appeared to offer greater local protection against infection than did the sulfanilamide films. Pickrell feels that these preformed films may find a definite place in surgery for the hospitalized and ambulatory patient and in cases in which infection is imminent and surface drying is desired or when moisture, coincident with the use of ointments and its resulting maceration, is to be discouraged.

California and Western Medicine, San Francisco

57:283-340 (Nov.) 1942

Hydatidiform Mole and Chorionepithelioma. M. Schulze, San Francisco.—p. 292.
War Dermatology: Some General Aspects. S. Ayres Jr., Los Angeles. —p. 294.
California State Board of Medical Examiners: How Funds Received from Physicians Are Expended. D. W. Stephenson, Sacramento. —p. 297.
War Gas Injuries of Eye. E. D. Godwin, Long Beach.—p. 299.
New Adrenalin-like Compounds: Their Action and Therapeutic Application. M. H. Nathanson, Los Angeles.—p. 301.
Thyroid in Pregnancy. C. J. Baumgartner, Los Angeles.—p. 307.
Tumors of Rectum. K. E. Smiley, Los Angeles.—p. 310.

Canadian Public Health Journal, Toronto

33:471-516 (Oct.) 1942

Scarlet Fever Immunization in Windsor, Ont. J. Howie, Windsor, Ont.—p. 471.
Food Consumption and Preferences of Families with Low Incomes in Halifax, N. S. E. G. Young, Halifax, N. S.—p. 480.
New Venereal Diseases Prevention Act of Ontario as It Affects the Medical Officer of Health. W. H. Avery, Toronto.—p. 486.
Interest of the Public in Health. D. W. Gudakunst, New York.—p. 490.
Plans for Vital Statistics. J. T. Marshall, Ottawa, Ont.—p. 495.

Endocrinology, Springfield, Ill.

31:573-702 (Dec.) 1942. **Partial Index**

Effect of Synthetic Desoxycorticosterone Acetate Therapy on Plasma Volume and Electrolyte Balance in Normal Dogs. M. Clinton Jr., G. W. Thorn, H. Eisenberg and Kay E. Stein, Baltimore.—p. 578.
Chemical Study of Tissue Changes in Adrenal Insufficiency and Traumatic Shock. A. P. W. Clarke and R. A. Cleghorn, Toronto, Canada.—p. 597.
Effects of Hormones on Erythropoiesis in Hypophysectomized Rat. E. P. Vollmer, A. S. Gordon and H. A. Charipper, New York.—p. 619.
Comparison of Thermostability of Growth and Ketogenic Activities of Anterior Pituitary Extract. R. A. Shipley, Cleveland.—p. 629.
Ultrafiltration of Anterior Pituitary Ketogenic and Growth Principles. R. A. Shipley and W. B. Seymour, Cleveland.—p. 634.
Action of Gynecogenic and Androgenic Hormones on Gonads and Pituitary Gland of Mature Male Rats. C. A. Joel, Basle, Switzerland.—p. 644.
Cardiotoxic Goiter: Distinct Entity: Preliminary Report. C. R. Schmidt and A. E. Hertzler, Halstead, Kan.—p. 684.

Florida Medical Association Journal, Jacksonville

29:199-246 (Nov.) 1942

Some Medical Problems of Flight. N. S. Rubin, Pensacola.—p. 213.
Shock. W. O. Arnold, West Palm Beach.—p. 219.
*The Sulfonamide Group in Surgery. F. J. Waas and E. Canipelli, Jacksonville.—p. 223.
Postpartum Hemorrhage. R. K. O'Brien, St. Petersburg.—p. 226.

Sulfonamides and Surgery.—In 100 consecutive surgical cases in which infection was established in 79 at operation and potential in 21, Waas and Canipelli applied the sulfonamide compounds locally whenever possible and also systemically by the oral or the parenteral route. The results in traumatic wounds and in intestinal anastomosis were extremely gratifying. In large, extensive surface wounds, exemplified by the radical mastectomy, there was a striking increase in bleeding and serum formation. The use of these drugs in such wounds has been discontinued. Primary closure and healing of infected wounds with the use of the drugs was most gratifying. Sodium sulfathiazole may be administered in a 0.5 per cent solution in isotonic solution of sodium chloride by hypodermoclysis. A stronger solution cannot be used beneath the skin. No severe or permanent adverse reactions were encountered.

Hawaii Medical Journal, Honolulu

2:1-52 (Sept.-Oct.) 1942

Disposition of War Casualties: War Wounds. A. W. Spittler, Honolulu.—p. 17.
Id.: Shock. C. T. Young, Honolulu.—p. 22.
Id.: Abdominal War Wounds. L. D. Heaton.—p. 26.
Id.: Chest Wounds. J. E. Strode, Honolulu.—p. 29.
Id.: Head Injuries. R. B. Cloward, Honolulu.—p. 32.
Id.: Orthopedic Wounds. J. D. MacPherson, Pearl Harbor.—p. 37.
Id.: Burns: Treatment Plan for Large Numbers. P. C. Spangler.—p. 40.
Id.: Blast Injury of Lungs; with Comment on Immersion Blast Injury. J. Palma, Pearl Harbor.—p. 42.

Journal of Experimental Medicine, New York

76: 497-598 (Dec.) 1942

Specific Polysaccharide Content of Pneumonic Sputums. J. T. Tripp; A. W. Frisch, Detroit; C. D. Barrett Jr., Mason, Mich., and B. E. Pidgeon.—p. 497.
Specific Polysaccharide Content of Pneumonic Lungs. A. W. Frisch, Detroit; J. T. Tripp; C. D. Barrett Jr., Mason, Mich., and B. E. Pidgeon.—p. 505.
Hypoproteinemia as Protection Against Mercuric Chloride Injury in Dogs. R. L. Holman, Chapel Hill, N. C., and G. L. Donnelly, Durham, N. C.—p. 511.
Low Protein Diet Augments Hyperproteinemia Produced by Repeated Injections of Homologous Plasma: Evidence for Dynamic Equilibrium Between Food, Plasma and Tissue Proteins. R. L. Holman, Chapel Hill, N. C.—p. 519.
Coagulation and Liquefaction of Semen: Proteolytic Enzymes and Citrate in Prostatic Fluid. C. Huggins and W. Neal, Chicago.—p. 527.
Natural Antibody That Reacts in Vitro with Sedimentable Constituent of Normal Tissue Cells: I. Demonstration of Phenomenon. J. G. Kidd and W. F. Friedewald, New York.—p. 543.
Id.: II. Specificity of Phenomenon: General Discussion. J. G. Kidd and W. F. Friedewald, New York.—p. 557.
Metabolism of Central Nervous System in Experimental Poliomyelitis. E. Racker and H. Kabat, Minneapolis.—p. 579.

Journal of Lab. and Clinical Medicine, St. Louis

28:127-254 (Nov.) 1942

Antibody Production and Anamnestic Reaction. P. R. Cannon, Chicago.—p. 127.
Sarcoidosis (Boeck-Besnier-Schaumann Disease) as Cause of Pituitary Syndrome. E. J. Kraus, Peoria, Ill.—p. 140.
Treatment of Congestive Heart Failure in Ambulatory Patients with Orally Administered Mercurial Diuretic. J. Burstein, G. Brown and C. Klein, New York.—p. 147.
Adenylic Acid and Bacterial Growth. S. Caspe and A. G. Osler, New York.—p. 150.
Fatal Salmonella Intracranial Infection in Infant: Report of Case. W. E. Bray and J. M. Meredith, University, Va.—p. 152.
Effect of Injection of Tissue Extracts on Number of Blood Platelets. A. Uihlein, Rochester, Minn.—p. 157.
*Preliminary Report on Treatment of Bacillary Dysentery with Succinyl Sulfathiazole. E. J. Poth, B. M. Chenoweth Jr. and F. L. Knotts, Baltimore.—p. 162.
New Hypothesis of Production of T Wave in Electrocardiogram Based on Electrokinetic Phenomena. J. R. Miller and R. F. Dent, Chicago.—p. 168.
Significance of Urinary Ammonia. A. P. Briggs, Augusta, Ga.—p. 174.
*Bromsulphalein Retention in Low Grade Chronic Illness. M. H. Stiles, M. T. Stiles and A. M. Kolb, Philadelphia.—p. 180.
Solubility and *pH* Data of Some Commonly Used Sulfonamides. W. G. Clark, E. A. Strakosch and N. I. Levitan, Minneapolis.—p. 188.
*Fat Metabolism in Acne Vulgaris. E. B. LeWinn and I. Zugerman, Philadelphia.—p. 190.

Treatment of Bacillary Dysentery.—The general regimen that Poth and his collaborators carried out in treating patients with bacillary dysentery included the administration of adequate parenteral fluids and electrolytes to combat dehydration when this was indicated, no transfusions of whole blood or plasma for the dysentery and succinyl sulfathiazole by mouth in a daily dose that varied from 0.25 to 1 Gm. per kilogram of body weight. The total daily dose was given in six equal portions. The length of treatment varied from two to seventeen days. There were no failures and no deaths. The ages of the patients ranged from 8 weeks to 83 years. The response of children and infants was prompt whether treatment was begun early or late in the disease. The response was equally good with small as well as with large doses. The temperature returned to normal in twenty-four hours or less in 9 of 10 instances. In the exception the time was thirty-six hours. The response of 10 adults to therapy was also prompt regardless of the duration of the disease. Bacteriologic studies showed that Shigella paradysenteriae was especially susceptible to the antibacterial action of succinyl sulfathiazole. The dysentery organisms ordinarily disappeared from the stools within forty-eight hours, whereas significant lowering of the coliform bacteria required two to three days of additional therapy. The drug was equally effective in the acute and the more chronic forms of the disease. No untoward toxic manifestations ensued.

Bromsulphalein in Low Grade Chronic Illness.—The hepatic function of 112 ambulant patients with low grade chronic illness probably secondary to chronic infection was determined by the Stileses and Kolb. The bromsulphalein test was used for the determination. Macdonald's normal criterion of complete elimination in twenty-five minutes of a dose of bromsulphalein equal to 5 mg. per kilogram of body weight was adopted. In all but 16 evidence of hepatic dysfunction was obtained. Of the remaining 96, more than 20 units of bromsulphalein was retained by 33. The mean retention of patients between 21 and 40 was less than the general average and that of patients more than 60 was greater, but the actual significance is uncertain. When the mean bromsulphalein retention of patients with mild general symptoms was compared with the mean retention of patients with moderately severe and severe symptoms, the differences were statistically significant, the respective values being 10, 18.9 and 44.7 units. While the bromsulphalein retention by patients with high sedimentation rates tended to be high, there were some with high rates whose retention was low and some with low rates whose retention was considerable.

Fat Metabolism in Acne Vulgaris.—LeWinn and Zugerman state that a study of the fat tolerance, indicated by blood cholesterol changes following the ingestion of fat, of 20 patients with acne vulgaris failed to reveal any difference from that of patients without acne.

Journal of Neurophysiology, Springfield, Ill.

5:417-520 (Nov.) 1942

Absence of Local Sign in Visceral Responses to Pain. D. G. Sattler, New York.—p. 417.
Potentials Recorded from Nerve Trunk and Dorsal Root by Micro Electrodes. H. O. Parrack, Boston.—p. 423.
Mediation of Descending Long Spinal Reflex Activity. D. P. C. Lloyd, New York.—p. 435.
Intersegmental Inhibition in Spinal Cord of Frog. H. Winterstein and M. Terzioglu, Istanbul, Turkey.—p. 459.
Oscillographic Studies on Spinal Tract of Fifth Cranial Nerve. F. Harrison and K. B. Corbin, Memphis, Tenn.—p. 465.
Effects of Intensity and Wavelength on Driving Cortical Activity in Monkeys. W. C. Halstead, G. W. Knox, J. I. Woolf and A. E. Walker, Chicago.—p. 483.
Reflex Discharges in Branches of Crural Nerve. B. Renshaw, New York.—p. 487.
Action Potential and Enzyme Activity in Electric Organ of Electrophorus Electricus (Linnaeus): I. Choline Esterase and Respiration. D. Nachmansohn, New Haven, Conn.; R. T. Cox, C. W. Coates, New York, and A. L. Machado, Rio de Janeiro, Brazil.—p. 499.

Journal of Nutrition, Philadelphia

24:405-502 (Nov.) 1942

Influence of Thiamine, Riboflavin, Pyridoxine and Pantothenic Acid Deficiencies on Nitrogen Metabolism. B. Sure and Z. W. Ford Jr., Fayetteville, Ark.—p. 405.
Inhibition of Symbiotic Synthesis of B Complex Factors by Sulfonamides. R. F. Light, L. J. Cracas, C. T. Olcott and C. N. Frey, New York.—p. 427.
Potassium, Sodium and Chlorine Balances of Preschool Children Receiving Medium and High Protein Diets. Jean E. Hawks, Merle M. Bray, Sylvia Hartt, Margaret Barry Whittemore and Marie Dye, East Lansing, Mich.—p. 437.
Riboflavin Requirement of Dog. R. L. Potter, A. E. Axelrod and C. A. Elvehjem, Madison, Wis.—p. 449.
Metabolism and Growth Rate of Rats. H. H. Kibler and S. Brody, Columbia, Mo.—p. 461.
Effects of Prolonged Daily Treatment of Normal Rats with Saline Anterior Pituitary Extract: I. Sexual Differences in Appetite, Growth and Organ Weights. L. Voris, M. Kriss, L. F. Marcy and R. S. Bowman, Philadelphia.—p. 469.
Id.: II. Protein and Energy Metabolism. L. Voris, M. Kriss, L. F. Marcy and R. S. Bowman, Philadelphia.—p. 481.
Effect of Vitamin B Deficiency on Intestinal Absorption of Galactose in Rat. A. H. Free and J. R. Leonards, Cleveland.—p. 495.

Journal of Urology, Baltimore

48:459-562 (Nov.) 1942

Urology in the Changing World. O. S. Lowsley, New York.—p. 459.
Large Bone Metastasis from Carcinoma of Ureter Complicated by Congenital Giant Hydronephrosis: Case. H. R. Sauer, Buffalo.—p. 467.
Ureterointestinal Anastomosis: Implantation of Double Ureter; Technic; End Result. L. R. Wharton, Baltimore.—p. 474.
*New Method of Ureteral Transplantation for Cancer of Bladder: Report of Fifteen Clinical Cases. H. J. Jewett, Baltimore.—p. 489.
Lymphosarcoma of Testis: Report of Four New Cases. M. B. Dockerty and J. T. Priestley, Rochester, Minn.—p. 514.
Humor of Spermatic Cord: Report of Case. V. F. Marshall, New York.—p. 524.
Lypomyxoma of Spermatic Cord: Case Report and Review of Literature. G. H. Strong, Baltimore.—p. 527.
Primary Malignant Tumor of Epididymis (Rhabdomyosarcoma). G. B. Strong, Baltimore.—p. 533.
Urinary Stress Incontinence: Its Relation to Cystocele and Lacerations of Pelvic Floor. J. W. Davies, New York.—p. 536.
Variation in Daily Urinary Excretion of Androgens in Relation to Benign Hypertrophy of Prostate. Mary L. Miller and R. A. Moore, St. Louis.—p. 544.
Properties of Organic Acid Solutions Which Determine Their Irritability to Bladder Mucous Membrane and Effect of Magnesium Ions in Overcoming This Irritability. H. I. Suby, R. M. Suby and F. Albright, Boston.—p. 549.

Ureteral Transplantation for Bladder Cancer.—Jewett designed a special electrode for establishing an adequate and permanent ureterointestinal ostium and then a simple two stage method of implanting two intact ureters simultaneously into the sigmoid in cancer of the bladder. He has completed both stages of the ureterointestinal implantation in 15 instances. Thirteen of the patients had extensive vesical carcinoma and 2 did not have cancer, so they consequently did not have cystectomy, but they fell in the same age group and were totally incapacitated by a deep seated infection of the bladder. Nine of the 15 patients are now living; the longest postoperative interval has been one and a half years. Of the 6 who died, 3 did so during convalescence and 3 after discharge from the hospital. In one of the hospital deaths the cause was attributable to an error in technic. An early model of the electrode did not work satisfactorily and extensive sloughing followed. The second patient died of sudden cardiac failure and the third of a volvulus of the lower ileum which was not related to the ureterosigmoidostomy. Of the 3 who died after discharge, 1 died in nine months from metastasis, 1 in six months from local recurrence of the carcinoma in the pelvis, probably with metastasis, and 1 died two months after operation; three weeks before death this patient's postoperative condition was excellent and there was no obstruction of the urinary tract. The attending physician thought that death was due to ascending renal infection. Necropsy was not obtained. The condition of most of the 15 patients was considered hopeless and every form of therapy had been tried elsewhere before transplantation of the ureters was done. The author believes that the mortality among patients of better surgical risk could be reduced considerably.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

50:543-596 (Nov.) 1942

New Surgical Technic for Resection of Skull: Introduction of Rotary Precision Cranial Saw. M. A. Glaser, Los Angeles.—p. 543.
Problem of Pulmonary Embolism. A. R. Barnes, Rochester, Minn.—p. 551.
*Use of African Clawed Frog (Xenopus Laevis Daudin) as Rapid Diagnostic Test for Pregnancy. A. I. Weisman, A. F. Snyder and C. W. Coates, New York.—p. 557.
Technic for Hofmeister Anticolic Gastric Resection. D. Metheny, Seattle.—p. 562.
Retrodisplacements of Uterus. L. C. Sheffey, Philadelphia.—p. 564.
Prevention of Obstetric Infection by Use of Vaginal Antisepsis. H. W. Mayes, Brooklyn.—p. 568.
Transnatal Asphyxia and Anoxia. C. J. Lund, Madison, Wis.—p. 575.
*Local Anesthesia in Obstetrics and Gynecology. J. P. Greenhill, Chicago.—p. 579.
Treatment of Prolonged Labor Due to Uterine Inertia. R. S. Siddall, Detroit.—p. 581.
Economics of Obstetric Care from Standpoint of Obstetrician. H. H. Cummings, Ann Arbor, Mich.—p. 588.

Frog Pregnancy Test.—Weisman and his colleagues have used the African clawed frog (Xenopus laevis, Daudin) in determining pregnancy in 267 women. In 154 the frog test was run parallel with the rabbit test and in 113 the tests were subsequently checked by physical observation and roentgenograms. The frog test was made with the urines of women who had missed not more than one menstrual period and who thought that pregnancy was possible. None could be diagnosed as pregnant or nonpregnant by physical examination. Of the 154 tested by both the rabbit and the clawed frog test, 148 were correctly diagnosed by both methods. The six discrepancies on further testing revealed the rabbit test to be in error in each instance. Of the 113 tested with the frog alone, 112 were diagnosed correctly and 1 incorrectly. The error was made on a woman who was seven days overdue in her menses; frog tests one week later showed a strong oviposition. The test has a number of advantages over other tests used for the diagnosis of pregnancy. It takes only six to twelve hours, it is 99.6 per cent accurate, it is simple to perform, the frogs are easy to maintain, the test is inexpensive as the animals can be used repeatedly, and the reading of the reaction is simply the gross observation of eggs in the water.

Local Anesthesia in Obstetrics.—Some of the advantages of local anesthesia in obstetrics and gynecology that Greenhill mentions are that there are practically no pulmonary, local or general complications, the mortality is negligible, there are no ill effects to the liver, lungs, heart, circulatory apparatus and central nervous system, bleeding in the field of operation is decidedly reduced, there is no asphyxia of the child, haste in operating is unnecessary and wound infection is decreased. Local anesthesia, the author states, should be used more widely by obstetricians and gynecologists, as it definitely decreases the mortality and morbidity. The obstetric indications are, in part, dilation and curettement for incomplete, missed and therapeutic abortion, hydatidiform mole, spontaneous delivery, episiotomy and repair, low forceps delivery, cesarean section and Porro operation. The gynecologic indications are dilation and curettement, plastic operations on the vagina, Manchester operation, Le Fort operation, vaginal hysterectomy, salpingectomy, oophorectomy and hysterectomy.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

54:255-282 (Oct.) 1942

Lichen Simplex Chronicus (Neurodermatitis) of Palms and Soles. Mary S. Smith.—p. 255.
Dermatomyositis: Case. Muriel J. L. Frazer.—p. 265.
Acne Vulgaris in Infants. R. Aitken.—p. 272.

British Journal of Surgery, Bristol

30:1-88 (July) 1942

Hemangiomas Arising in Bones of Skull. G. F. Rowbotham.—p. 1.
*Fatigue Fracture of Tibia. J. B. Hartley.—p. 9.
Ileogastric Syndrome. L. R. Braithwaite.—p. 13.
Ectopia Vesicae Complicated by Adenocarcinoma, with Review of Literature. W. H. Graham.—p. 23.
Morbid Anatomy of Case of Recurrent Dislocation of Shoulder. A. L. Eyre-Brook.—p. 32.
*Blast Effects in Warfare. E. R. P. Williams.—p. 38.
*Pathologic Changes Produced in Animals by Depth Charges. G. R. Cameron, R. H. D. Short and C. P. G. Wakeley.—p. 49.
Fibrous Stricture of Small Intestine Following Strangulated Hernia. H. C. Barry.—p. 64.
Traumatic Rupture of Urethra. M. Silverstone.—p. 70.

Fatigue Fracture of Tibia.—Since 1931 Hartley has seen 14 patients complaining of pain in the calf or near the upper end of a tibia, and generally to the inner side. There is little to see or feel and roentgen study reveals changes which, in an early case, suggest an incomplete tibial fracture from 2½ to 3 inches below the knee joint. A small knuckle of callus is usually visible at the inner or posterior aspect of this level. In 3 patients the condition was bilateral, which observation can lead only to the diagnosis of fatigue fracture in a person between 7 and 20 years of age. The most recent case has demonstrated the need for recognizing this condition during war, for in this instance an erroneous diagnosis led to severe fracture of the tibia and fibula in an active recruit, and consequently to prolonged immobilization. Now that adolescent groups are liable for war service, the incidence is likely to be greater, since fatigue fracture is more common in adolescence. Generally there is no history of injury or of violence. Nine of the author's 14 patients had no history of injury, 4 had a history of a recent fall or blow and 1 thought he had fallen. The only constant symptom is pain on standing, on walking or after walking. This may be either behind the knee, in the calf or over the inner aspect of the upper third of the tibia. There is no pain when the leg is at rest. So far no patient with bilateral involvement has complained of pain in both legs. Slight swelling on the inner aspect of the upper end of the shaft of the tibia was present in only 5 cases and tenderness in 3. Spontaneous cure results from nothing more than rest from weight bearing for several weeks. The condition may be due to faulty crystal structure of bone at this area of maximal strain and/or to abnormal strain at an already considerably weak site. It is essentially a fatigue dystrophy. Its roentgen appearance and healing are similar to march fracture of the metatarsals. It is not due to infection, bone tumor, Looser's umbauzonen, syphilis or tuberculosis.

Blast Effect in Warfare.—Williams believes that it is important to determine which of the three components in the compound blast wave in air is the traumatic factor and how it affects the body. The effect of the negative air suction wave cannot be neglected. This wave has a great amplitude, as it starts at the peak of the positive pressure and descends slowly to below atmospheric pressure. Sudden decreases in air pressure, the negative phase of the blast wave, is certainly likely to be injurious to human lungs already damaged by the positive phase. The third blast component of mass movement of air or gas is capable of inflicting injury and is responsible for the shattering effects produced in the immediate vicinity of an explosion. In water, where mass movement is of a small degree even in close proximity to an explosion, these shattering effects are not observed. Contusional effects can be produced by the rush of gas from an explosion irrespective of any damage which the pure pressure wave may have caused. The lesions caused in water are due to a single high pressure wave, and there is no question of a wave descending the trachea or an after suction wave. The effects on the body of explosions, both in air and in water, are primarily due to the externally applied pressure wave, but in air both the windage factor and the after suction waves play their part. Internal injury due to blast without external marks of violence is rare. Only 4 such cases were encountered among 1,500 casualties—in practically every instance a coexisting wound due to crushing, asphyxia and the like will be evident.

Depth Charges and Pathologic Changes.—Should a depth charge, mine or torpedo explode in the vicinity of where a ship's company is in the water after the sinking of their ship there is grave danger of most of the men losing their lives. The clinical manifestations of patients who have suffered from water blast vary from slight spinal concussion accompanied by bloody diarrhea to laceration of the abdominal organs and lungs. The mortality from water blast is high and it is conceivable that many war casualties are due to this factor alone. With the object of finding out the real causation and mechanism of the thoracic and abdominal lesions and also to see if any form of simple protection could be devised, Cameron and his collaborators carried out a series of animal experiments. Microscopic examination has confirmed naked eye observation that the most important structural changes produced by a depth charge are in the respiratory system. There is a striking similarity in the nature of these effects, the main variation being in their intensity and distribution. The pulmonary changes are hemorrhage and emphysema with rupture of air spaces. Study of the pulmonary changes leads to an elucidation of the mechanism of depth charge effects. The most severe injury was seen in animals which were within a radius of 40 yards from the depth charge. Eleven of 13 animals within this radius were killed instantly; 10 showed extensive pulmonary hemorrhage and 5 moderate to severe interstitial emphysema. Hemorrhage may, however, develop in animals as far away as 100 yards. Severe pulmonary hemorrhage may occur without immediate death, while animals may be killed at once and not show definite pulmonary lesions. Hemorrhage is present more frequently in the right than in the left lung; the upper lobes and margins of the lung are the most common sites involved. Bronchi may become filled with large blood clots, while small hemorrhages sometimes develop in the walls of the trachea and bronchi. Acute vesicular and interstitial emphysema are practically constant in animals within 40 yards of the depth charge. Emphysema affects the upper lobes of both lungs most often, being least frequent in the lower lobes. Pneumothorax and hemothorax are sometimes concomitant. Little damage is produced in the soft structures of the wall of the body and the bones. There is no special tendency for certain hollow viscera containing fluid, such as the gallbladder and urinary bladder, to be involved.

British Medical Journal, London

2:505-534 (Oct. 31) 1942

*Nutritional Iron Deficiency Anemia in Wartime: I. Hemoglobin Levels of 831 Infants and Children. L. S. P. Davidson, G. M. M. Donaldson, M. J. Dyar, S. T. Lindsay and J. G. McSorley.—p. 505.
*Plasma Protein Storage. J. Beattie and H. B. Collard.—p. 507.
Tonsillectomy by Guillotine and Dissection. T. B. Jobson.—p. 512.
Atypical "Influenza Pneumonia" at a School. H. G. J. Herxheimer and A. J. McMillan.—p. 513.

Nutritional Iron Deficiency Anemia.—Davidson and his colleagues assessed the iron deficiency of 442 infants and preschool children from 2 to 4 years of age and of 389 children from 5 to 12 years of age attending two primary day schools in Edinburgh. A comparison of the hemoglobin levels of children 2 to 23 months of age in the present Edinburgh series with the figures for an Aberdeen series indicates that the incidence of severe anemia (less than 61 per cent of hemoglobin) in the 1935 Aberdeen series is three times as great as in the 1942 Edinburgh series, but the proportion of moderately anemic infants (61 to 70 per cent of hemoglobin) has risen by 10 per cent in Edinburgh as compared with the Aberdeen figure. Eighty-three per cent of the Edinburgh infants and 87 per cent of the Aberdeen infants have a hemoglobin level of less than 80 per cent. After three years of war there has been no deterioration in hemoglobin levels, but anemia is still common. Any advantage which the Edinburgh has over the Aberdeen series in infancy appears to be lost during the preschool or the 2 to 5 year period. Thus on

entering school at 5 years the Edinburgh children had an average hemoglobin of 81 per cent compared with an average figure of 87 per cent for the Aberdeen series. Only 9 per cent of 197 school children had hemoglobin levels of 90 per cent. The hemoglobin levels of children reaching school age were slightly lower in the Edinburgh series than in the prewar Aberdeen series. More than half of the children in the Edinburgh series had hemoglobin concentrations below 80 per cent. The frequency and degree of anemia in these school children call for the most careful consideration by both local and national authorities. During the period of active growth and mental development the incidence of anemia should be reduced to the lowest possible level. This can be achieved by the provision of school meals which are appetizing, well balanced and rich in foodstuffs with a high iron content and/or by supplying iron to the children in the form of a tablet or a mixture or incorporating it in some universally eaten food, such as bread.

Plasma Protein Storage.—To determine plasma protein storage Beattie and Collard studied the effects of plasma transfusions on hepatectomized and anesthetized cats and of varying protein concentrations in the perfusing fluid in perfused isolated liver. After repeated transfusions with plasma of a protein content lower than that of the animal's blood, the plasma protein rose significantly in 4 of the 5 animals, and the rise in 1 was of doubtful significance. Four animals lost the major portion of the transfused fluid from the circulation. One animal lost about half the transfused fluid. The plasma protein added to the blood was retained in the circulation in 2 animals and considerable fractions of it left the circulation in the others. Presumably the greater part of this "lost" protein entered the protein stores. Retention of plasma protein in the circulation may be accomplished by increasing the concentration to a much higher level and by expanding the blood volume. The isolated liver experiments show clearly that the liver can mobilize and throw into the perfusing fluid quantities of plasma protein. The stimulus for this production is obviously the low plasma protein concentration of the perfusing fluid. There was also a correlation between the degree of "hypoproteinemia" and the rate of plasma protein production. When plasma was added to the perfusing fluid about one hour after the experiment had begun the results obtained seemed to depend partly on the state of the reserves and partly on the concentration of protein in the perfusing fluid. There can be no doubt that the liver is a "store" for plasma protein, but to determine if it was the only store hepatectomized animals were prepared and after variable periods given plasma. Two animals showed no change in total plasma proteins before they were given a transfusion, seventy minutes after the transfusion 1 showed an appreciable loss of protein out of the circulation, 1 lost a greater amount in forty minutes and 1 had lost some protein before transfusion and continued to lose an even greater quantity afterward. This may suggest a movement of protein into other stores, but they are not as convincing as evidence of movement from such stores into the blood. Such evidence is provided by 2 cats; in 1 over a period of thirty minutes while blood dilution was proceeding, the total plasma protein was raised by a small but significant amount, and in 1 over a period of forty-five minutes while blood dilution was proceeding, the total plasma protein was raised by 11 per cent over the expected value. In the first animal the addition of protein to the circulation continued after a plasma transfusion at about the same rate as before transfusion. The evidence suggests that plasma protein leaves the blood stream in hepatectomized animals in quantities greater than might reasonably be required for normal metabolism and, conversely, these animals seem to possess some source of plasma protein other than the liver. Whether all body cells can contribute protein to the blood stream with the facility with which they can apparently withdraw it has yet to be decided.

Edinburgh Medical Journal

49:593-656 (Oct.) 1942

The Medical Preliminary and After. S. McDonald.—p. 593.
Problem of Air Borne Infection. T. J. Mackie.—p. 607.
Treatment of Cerebrospinal Fever with Sulfapyridine. A. Joe.—p. 628.
Payments by Patients in Eighteenth Century. D. Robertson.—p. 643.

Schweizerische medizinische Wochenschrift, Basel

72:661-684 (June 20) 1942. **Partial Index**

Relation Between Muscular Fatigue and Adrenals, with Theory of Muscular Contraction. F. Verzár.—p. 661.
Prophylactic Inoculations. E. Berger.—p. 668.
*Pathogenesis of Hypochromic Anemia Following Gastric Resection. G. Hemmeler.—p. 670.
Determination, Distribution and Elimination of Acetylsulfanilamide in Man. E. Deutsch.—p. 672.

Pathogenesis of Hypochromic Anemia Following Gastric Resection.—Attention has frequently been called to the frequent occurrence of anemia, particularly hypochromic anemia, following resection of the stomach for gastroduodenal ulcer. It was assumed that iron deficiency was the cause. According to Hemmeler, anemia due to iron deficiency following gastric resection can arise (1) from a deficiency of hydrochloric acid in the stomach. Study of the gastric juice of patients who had stomach resection revealed achylia in from 80 to 95 per cent of the cases reported by various authors. Anemia due to iron deficiency may also be due (2) to too rapid gastric passage of the alimentary mass, so that the alimentary iron has not sufficient time to become transformed into an absorbable ionized form. It may be due (3) to the fact that the alimentary mass no longer passes into the duodenum, the site of the assimilation of iron. The author studied these factors with the aid of absorption curves for iron. His investigations reveal that the anacidity or hypoacidity of the gastric juice diminishes the ionization of the alimentary iron which is indispensable for iron absorption. The accelerated gastric passage of the alimentary mass likewise plays a part, because the iron, even in the presence of hydrochloric acid, does not have the time to become ionized. The fact that the food does not pass the duodenum, the usual site of iron resorption, is of no importance in the pathogenesis of anemia following gastric resection because ionized iron can be absorbed below the duodenum. Occurrence of hypochromic anemia after gastric resection can be prevented by administration of iron as soon as the serum content of iron shows diminution.

72:685-728 (June 27) 1942. **Partial Index**

Epidemiology of Tuberculosis in Denmark. T. Madsen.—p. 685.
*Late Primary Tuberculous Infection and Its Development. W. Löffler. —p. 686.
*Late Primary Tuberculous Infection and Its Early Evolution. E. Uehlinger.—p. 701.
*Late Primary Tuberculous Infection and Its Development. S. J. Leitner. —p. 711.
Severe Tuberculous Familial Infection. A. Wernli-Hässig.—p. 713.
Prognosis of Pulmonary Tuberculosis: Weltmann Reaction Carried Out with Citrated Blood. J. Stephani.—p. 716.
Reduction of Temperature by Sulfanilamide as Differential Diagnostic Characteristic, Particularly Against Tuberculosis. J. L. Burckhardt. —p. 717.

Late Primary Tuberculous Infection.—According to Löffler the less rapid spread of tuberculosis in the population has delayed the primary infection of many persons into adulthood. In Switzerland the primary infection of adults follows the same course as in children. It presents no sharply outlined symptomatology but rather a heterogeneous picture. Many primary infections run their course unobserved; only a small number cause clinical manifestations. Some cases exhibit only roentgenologic changes; others appear as febrile conditions with many possible diagnostic explanations. In the presence of an obscure febrile condition a primary infection should be thought of. The clinical symptoms of erythema nodosum (with or without Poncet's rheumatism and phlyctenae) and of exudative pleurisy of adults, particularly of young adults, are often a typical expression of a primary infection. Tuberculous infiltrates of adults represent particularly typical manifestations of primary infection rather than of secondary infiltrations or of early infiltrates. They are of exogenic origin and call for isolation and examination of persons in their environment. Today it is necessary to prove secondary infiltrations, whereas until recently it was necessary to prove primary infiltration. The demonstration of tuberculous exposure supports a suspected diagnosis. Intestinal primary infection must be considered in some cases, although it is rare. The frequent observation of primary infection in military service involves no decisive changes in insurance compensation because when acute extensive dissemina-

tion, pleurisy and erythema nodosum occurred during service or shortly thereafter compensation was granted on the basis of the principle of contemporaneity.

Late Primary Tuberculosis and Its Early Evolution.—Uehlinger points out that the gradual increase in late primary infections is a result of the gradual decrease in the tuberculous involvement in children. On the basis of postmortem observations in the army, evidence of tuberculous infection can be expected in approximately 50 per cent of the age groups between 20 and 55 years. The importance of late primary tuberculous infection is proved by the fact that, of 72 fatal cases of miliary and meningeal tuberculosis observed from 1939 to 1941, 60 could be traced to a late primary infection. In contradistinction to postmortem studies, the clinical diagnosis of a late primary tuberculous infection is extremely difficult. The majority (about two thirds) of late primary infections pursue a silent course. Only the postprimary hematogenic and canalicular dissemination of the infection generally leads to clinical manifestations. The most frequent forms of benign, hematogenic early evolution are erythema nodosum and exudative pleurisy; the most frequent malignant form is the progressive protracted dissemination with terminal tuberculous meningitis and miliary tuberculosis. The source of dissemination is frequently the cavernous breakdown of the primary infiltrate or of a tracheobronchial lymph node perforating into a bronchus. Early malignant evolution of a late primary pulmonary infection must be suspected in the presence of progressive loss of weight, prolonged acceleration of the sedimentation rate, progressive leukopenia with lymphopenia, tachycardia, persistence or greatly retarded absorption of the primary infiltrate, and recurrent febrile bacillemia. Primary infection during adolescence has a comparatively high mortality, because at this time of life there is a predisposition to hematogenous dissemination. High mortality rates are to be expected if late primary infection becomes frequent among a population with a low index of infection. Late primary infections require careful supervision. They suggest the presence of persons with open tuberculosis in the environment.

Late Primary Tuberculosis and Its Development.—Of Leitner's 48 patients with late primary infection, 37 complained of fatigue; 16 had cough, 2 expectoration and 33 fever. Sensitivity to tuberculin was pronounced in all. Erythema nodosum was observed in almost one third. While erythema nodosum is not a specific tuberculous lesion, it is seen in the majority of cases. The frequency of erythema nodosum during the primary infection and the pronounced tuberculin sensitivity indicate early development of an intense allergy. Erythema nodosum is probably to be regarded as an allergic reaction. The author differentiates primary infection into (1) a clinically, as well as roentgenologically, latent type recognizable only by the fact that the tuberculin reaction becomes positive, (2) a type clinically latent but with a positive roentgen picture, (3) a type with clinical and roentgenologic manifestations resembling an acute infectious disease and (4) a type with clinical signs but atypical roentgen picture. This last type can be recognized only by the positive tuberculin reaction. The author gained the impression that allergy is usually most pronounced shortly after primary infection. As regards immunity he believes that there is practically no superinfection during the biologic activity of tuberculosis recognizable by the positive tuberculin reaction. The author stresses the advantages of tuberculin tests in large groups (universities, armed forces, occupational schools and factories). It is simple, reveals sources of infection and makes possible early treatment.

Anais Brasileiros de Ginecologia, Rio de Janeiro

14:1-80 (July) 1942. **Partial Index**

Hyperplasia of the Endometrium. T. S. Cullen.—p. 1.
*Chorea in Pregnancy: Vitamin B_6 Therapy. S. Rabin and H. Duék. —p. 12.

Chorea in Pregnancy.—Rabin and Duék direct attention to the therapeutic value of vitamin B_6 in chorea of pregnancy. They believe that chorea of pregnancy and chorea minor have a common etiology, namely avitaminosis B_6, and that the etiologic therapy in either type consists of administration of vitamin B_6. A primipara aged 19 reported to the hospital during the second month of pregnancy complaining of vomiting. Emesis was controlled by endocrine therapy. Shortly afterward chorea developed. The treatment consisted in intramuscular injections of 50 mg. of pyridoxine given daily for a week and every other day for another week. The total number of injections was ten. The patient was given a diet rich in vitamins. Chorea was rapidly and permanently controlled. The appetite of the patient and her general condition rapidly improved.

Revista Clínica Española, Madrid

5:161-226 (May 15) 1942

Physiopathologic Studies of Thymus and Its Hormone. P. Farreras Valenti.—p. 161.
Investigations on Lathyrism. C. Jiménez-Diaz, E. Roda, E. Ortiz de Landázuri, C. Marina and L. Lorente.—p. 168.
Roentgenologic Study of Ulcers of Pyloric Passage. L. de Lara.—p. 177.
*Arteriography in Osseous Lesions. F. López Areal.—p. 182.
Dietic Insufficiency as Cause of Extrapyramidal Symptoms. J. Calvo Melendro.—p. 185.
*Study of Disturbances in Aviators During Acrobatic Flight: Cerebral Factor. L. Pescador.—p. 190.
Nicotinic Acid in Cerebral Thrombosis. D. Furtado.—p. 193.
Sulfonamide Therapy in Streptococcic Meningitis of Otogenic Origin. R. Álvarez Pérez.—p. 195.

Arteriography in Bone Lesions.—López Areal advocates injection of from 10 to 20 cc. of a 35 per cent solution of sodium iodide. This substance produces no changes in the vascular endothelium as demonstrated by surgical interventions. Arteriography is of diagnostic value in all bone lesions. To facilitate the exact diagnosis it is important to study the collateral circulation. In benign bone tumors the collateral circulation shows no alteration either in caliber, direction or form of the main vessel, although occasionally the vessel becomes slightly displaced by the tumor. In malignant tumors, particularly sarcomas, the collateral circulation always shows abnormal increase; the vascular net is complicated; branches cross aimlessly without any arrangement, newly formed vessels of irregular distribution course in all directions and there are vessels which supply the tumor. Veritable pools of blood exist in telangiectatic tumors and make the roentgenogram appear cloudy. The appearance and extent of the collateral circulation are the chief guide in the differential diagnosis between neoplastic and nonneoplastic bone lesions and between benign and malignant bone tumors. Arteriography is also a valuable aid in the control of the roentgen irradiation of bone tumors.

Cerebral Disturbances in Aviators During Acrobatic Flights.—Pescador mentions the various aspects of acceleration disease and emphasizes that a cerebellar component exists in the disturbances that develop during acrobatic flights. This cerebellar component is manifested by static changes, by mild disturbances in walking and in coordination, by tremor and by hypermetria. In animal experiments changes become evident which indicate disturbances in the inferior nuclei demonstrated by the abolishment of certain statokinetic reflexes. It is suggested that the blood perfusion of the dentate nucleus, which is the weakest point in the cerebellar economy, assumes a decisive role in the pathogenesis.

Revista de la Facultad de Medicina, Bogotá

10:435-498 (April) 1942. **Partial Index**

*Transmission of Leprosy by Fleas: Some Observations. G. Muñoz Rivas.—p. 635.
Dementia Paralytica, Tabes and Diabetes Insipidus. A. Hernández. —p. 680.

Transmission of Leprosy by Fleas.—Muñoz Rivas found that when fleas of the type Pulex irritans and Pulex canis bite patients with leprosy they suck up lepra bacilli which will survive for more than twenty-six hours in the digestive tract of these insects. The stomach of larvas fed on dejecta of adult fleas biting patients with leprosy contain acid alcohol resistant bacilli in 21 per cent of the cases. The stomach of larvas fed on infected leprous food contain lepra bacilli in 100 per cent of the cases. The stomach of larvas from fleas captured in the rooms of patients with leprosy or which were left in contact with earth from the rooms of these patients contain acid alcohol resistant bacteria morphologically identical with lepra bacilli in 75 per cent of the cases. The author concludes that fleas transmit leprosy. Extermination of fleas should be a part of the campaign against leprosy.

Book Notices

Sulfanilamide and Related Compounds in General Practice. By Wesley W. Spink, M.D., F.A.C.P., Associate Professor of Medicine, University of Minnesota Medical School, Minneapolis. Second edition. Cloth. Price, $3. Pp. 374, with illustrations. Chicago: Year Book Publishers, Inc., 1942.

A subject of the greatest interest to all practitioners of medicine is the use of the various sulfonamide compounds in the treatment of infections. Indeed, no aspect of medicine has attracted wider attention during the past few years. In this edition of Dr. Spink's monograph there is presented in a simple, direct and clear style a summary of sulfonamide therapy which should be read by every student of the subject and every practitioner of medicine who uses these important therapeutic agents. The text shows a sense of critical method which is invaluable to the reader, and many of the case reports which are based on the author's personal experience are illustrated by good charts. Dr. Spink has done a splendid piece of work and the medical profession is indeed fortunate to have such an authoritative and up to date monograph on the sulfonamides available as a guide to treatment.

How to Be Fit. By Robert Kiphuth, Director of the Gymnasium, Associate Professor of Physical Education, Yale University, New Haven. Foreword by John Kieran. Cloth. Price, $2. Pp. 131, with illustrations. New Haven: Yale University Press, 1942.

The book is a well written, well edited collection of exercises directed toward physical development. The purpose of the exercises is to work all muscles of the body including some that are little used. The exercises do not call for sudden strain nor do they tax the body unduly. There are two sets of lessons. Each lesson is composed of eight exercises, with excellent illustrations of each. The first set of lessons numbers fifteen and is designed for general use of old and young. Any one who plays golf or tennis or does gardening can do them. The second set of five lessons is a sort of "postgraduate" course, to be used on completion of the first set and only by the young and strenuous who wish further development. The book is well worth while for use in gymnasiums, schools, Y. M. C. A.s and colleges. The author is an authority on the subject, having been the director of gymnasiums and swimming coach at Yale for twenty-five years. The book is the result of his experience.

Manual of Dermatology. By Donald M. Pillsbury, M.D., Marion B. Sulzberger, M.D., and Clarence S. Livingood, M.D. Military Medical Manuals. Issued under the Auspices of the Committee on Medicine of the Division of Medical Sciences of the National Research Council. Cloth. Price, $2. Pp. 421, with 109 illustrations. Philadelphia & London: W. B. Saunders Company, 1942.

As the material in this manual is designed for the use of medical officers, the text concerns itself only with the management of the dermatoses commonly encountered in the armed forces. Consideration is not given to rare or obscure dermatoses or to those affecting particularly women, children or the aged.

The authors have designed a textbook which will be most useful for the diagnosis and treatment of the vast majority of the cutaneous disorders encountered. The early chapters cover the general considerations of diagnosis, with due emphasis on the history and the clinical findings with regard to primary and secondary lesions and the distribution of the lesions. Then follows a chapter which deals with the sites commonly involved in a number of dermatoses. This material is presented chiefly by means of fourteen full page illustrations which demonstrate graphically the topographic tendencies of some sixteen dermatoses and twenty-seven types of involvement of the mucous membranes.

The common disorders are then considered individually from the standpoints of clinical findings, differential diagnosis and treatment. These descriptions are concise but contain a maximum of information. A particularly valuable feature in this section is the use of numerous inserts which emphasize important fundamental features in the various diseases and which furnish guideposts designed to avoid common errors in diagnosis and treatment.

The material dealing with treatment includes a chapter on the general principles of local treatment and consideration of simplified and of extended therapy, the latter for use in hospital or sick bay. In addition an appendix furnishes a formulary of eighty-two prescriptions of tested merit.

All the clinical illustrations are grouped in one section of seventy-eight pages; these have been well selected, and salient diagnostic features are pointed out in the legends.

The authors have used their material in so ingenious a manner that a vast amount of information has been compiled in a small space, and the manual should have a great appeal for physicians both in military and in civil practice of medicine.

Blenorragia y sulfamidas. Blenorragia: Nociones generales de diagnóstico; tratamiento actual. Sulfamidas: Estudio clinico experimental. Sulfamidoterapia en la blenorragia. Por Guillermo Iacapraro, profesor adjunto de la facultad de ciencias médicas de Buenos Aires. Tesis de profesorado. Paper. Pp. 562, with illustrations. Buenos Aires: Imprenta Ferrari Hnos., 1941.

The subject matter consists chiefly of the diagnosis and modern treatment of gonorrhea, with clinical and experimental data. Of great interest are those sulfonamide compounds not generally used in the United States, such as uliron, neo-uliron, albucid and rodillone. With uliron Scherber and, independently, Löhe and his co-workers are quoted as claiming 75 per cent cures in 75 and 98 cases respectively. But the author obtained in 54 cases only 19 cures. In 11 per cent of these, prostatitis and epididymitis developed during treatment. With albucid the author quotes von Kennell as curing 86.5 per cent of 200 cases and St. Wolfran of Vienna as curing 98 per cent of 81 cases treated. The author himself, however, finds this drug less effective than sulfapyridine, even though better tolerated. Rodillone has been considered of value by Heitz-Boyer. Durel, however, obtained only 20 per cent cures and felt that the compound's greatest value was in subacute cases. Saby stressed the early use of rodillone. If there was no response in a week the drug was discontinued.

Illustrations showing the gross and microscopic lesions in intoxication with these compounds are excellent. Experiments were carried out on a series of 55 rats to demonstrate lesions of the gastrointestinal tract and other organs. The changes in the stomach varied from simple erosion to ulcerative necrosis. Chronic intoxication was manifested as chronic inflammation. No lesions were found in the control animals or in animals receiving subtoxic dosage. Sulfapyridine brought about the severest reaction. In decreasing severity red prontosil, uliron and white prontosil produced superficial lesions. No lesions occurred with albucid, septazine, sulfathiazole and neo-uliron. The author concludes that sulfapyridine is contraindicated for patients with inflammatory and ulcerative gastric lesions.

Normal and pathologic tissue cultures containing a 1 per cent concentration of the various sulfonamide compounds were studied. The sulfonamides did not produce definite cytolysis or inhibit the growth of either the normal or the pathologic (fusicellular sarcoma of the rat) tissue in this concentration. The monograph is a complete treatment of the subject up to and including the introduction of sulfathiazole.

This Is My Life. By Agnes Hunt, D.B.E., R.R.C. Foreword by Morris Bishop. Cloth. Price, $2.50. Pp. 27, with drawings by Georg T. Hartmann. New York: G. P. Putnam's Sons, 1942.

Agnes Hunt in 1900 founded the first open air orthopedic hospital. The Boschurch Home was then an old farm house in a village in England. In less than forty years the home had become a hospital of more than 300 beds with orthopedic clinics stretching out over eight counties, a staff of after-care nurses and a training college for cripples. By 1901 the stable about the old home had become the plaster room, the coach house the splint shop, the saddle room a bathroom, the cow houses a laundry, and the pigsty, after many vicissitudes, was turned into a sitting room. Nevertheless the home had an attraction for cripples. The author, who was a cripple, was advised to consult Mr. Robert Jones, the great orthopedic surgeon of Liverpool. This day in 1903, she says, was the greatest day of her life, even though it was followed by three months in a "Jones abduction frame." Robert Jones later came to the countryside in consultation and on his way paid a visit to the Boschurch Home.

When no one descended from the train at the stop, the great specialist was found comfortably asleep in the train. Thus Robert Jones became interested in the home and for nearly thirty years thereafter "worked for us and loved us even as we well-nigh worshipped him." It was his genius and great spirit which developed this home into a vast hospital, which shortly after Sir Robert's death was named the Robert Jones and Agnes Hunt Orthopedic Hospital. Sir Robert died on Jan. 18, 1933. Agnes Hunt wrote this book to amuse him in his last illness. No doubt Sir Robert was amused by Agnes Hunt's tales of her remarkable mother, whose size, it is said, was equaled only by her iron whims and determinations and who with whirlwind energy "managed family perils, domestics, animals, storms and continents." Mamma Hunt transported her large family to Australia to raise angora goats, only to learn on arrival that no one there had ever seen an angora goat. After difficult years in Australia the family returned to England by way of the United States and decided to start a convalescent home. This book should interest nurses particularly. The dean of Durham, the Rev. C. A. Allington, author of "Poets at Play," offered to refund the purchase price of the book to any one who did not feel happier and better for reading it.

Personal and Community Health. By C. E. Turner, A.M., Sc.D., Dr. P.H., Professor of Biology and Public Health in the Massachusetts Institute of Technology, Cambridge. Sixth edition. Cloth. Price, $3.50. Pp. 652, with 131 illustrations. St. Louis: C. V. Mosby Company, 1942.

This edition of Turner's standard textbook is satisfactory. It follows the conventional textbook arrangement with part one devoted to personal health, part two to community health, appendix A to communicable diseases and appendix B to an evaluation of disinfection methods and materials. The material is sound, well selected and clearly presented. Professor Turner gives perhaps more anatomic basis than most writers on personal and community health. The book covers fully the important questions of health values, nutrition, digestion, oral hygiene, respiration, circulation, excretion, endocrines, special senses, mental hygiene, exercise, body mechanics, foot hygiene, reproduction, heredity, narcotics and stimulants, and responsibility for health maintenance as factors in the individual health. Under community health will be found discussions of disease prevention, communicable diseases, immunity, specific diseases, food control, water supply, waste disposal, ventilation, heat and light, public health administration, maternal and child health, and school and industrial hygiene. There are 127 illustrations in black and white and 4 color plates. There is a good glossary and an adequate index. The book can be recommended for its thoroughness, reliability and clearness.

Her Star in Sight: Mary Carstens in Medical School. By Mildred Foulke Meese. Cloth. Price, $2. Pp. 331, with illustrations by Sandra James. Indianapolis and New York: Bobbs-Merrill Company, 1942.

This is a romantic story of Mary Carstens, who decided while still in high school that she wanted to be a doctor. Mary had lived for many years in an orphanage. Now we see her in medical school, in the sorority house, in the hospital wards as a student and through her internship, graduation in medicine and state board examinations. Mary was in love with young Dr. Peter Kirkland, who after the attack on Pearl Harbor was commissioned a major in the medical corps with the Marines. Fortunately Peter was able to attend Mary's graduation in his uniform before leaving for military duty and they became engaged. Before writing this novel the author visited hospitals, laboratories and classes in medical schools and studied medical records. It has, therefore, some medical background and should interest girls who have an ambition to study medicine.

His Sword: A Tale of the Vikings. By Alfred C. Muller, M.D. Cloth. Price, $2. Pp. 246. Boston: Meador Publishing Company, 1942.

Years ago a sunken ship was discovered near Oeseberg, Norway, which was the grave of King Harold's daughter, Queen Asa of Viken, and her favorite handmaiden, who had been killed in order that she might serve her mistress in Valhalla, as was the custom of those times. This ship is now in a museum in Oslo. The author, a country doctor now 76 years of age, began to write a historical novel based on this discovery, but as he delved into history it appeared that Queen Asa had done away with her husband and therefore did not deserve the service of a lovely handmaiden in Valhalla or the sacrifice of her life in order to serve the queen. The author then abandoned the strictly historical outline and wrote a fanciful story in which he makes the queen a heroine and spares the life of her handmaiden. The book takes its title from the great sword Sunderer, with which it was believed no brave king could ever lose a battle. When King Erling died he bequeathed the great sword to his young son Ottar, who swore to forge the Northland into a united kingdom. At the same time the tender youth laid the foundation for a psychic inhibition which ardent love for his queen could not overcome. The author shows an insight into human nature throughout the book. His style and choice of words are well adapted to a story of the hardy vikings.

The Making of a Surgeon: A Midwestern Chronicle. By Ernest V. Smith, M.D., D.Sc., F.A.C.S. Cloth. Price, $3. Pp. 344, with illustrations. Fond du Lac, Wis.: Berndt Printing Company, 1942.

At 23 the author decided to study medicine even though it was necessary to work his way through medical school. After graduating in 1907 at the University of Minnesota and without having an internship, he married the girl he had been courting for many years and went into practice in a small town. Four years later he accompanied a patient to the Mayo Clinic, where his former instructor Dr. Louis B. Wilson suggested that he come to the clinic to work for three years, one in pathology, one in internal medicine and one in surgery. "Then," Dr. Wilson said, "you will be a real doctor." The author followed this advice. He established a clinic in Fond du Lac, Wis., in 1916 in partnership with other physicians, three of whom are still there after more than twenty-five years, a period, the author says, longer than any other three doctors have worked together in the same capacity in the history of medicine and surgery. These men are Dr. Oliver M. Layton, Dr. William J. Waldschmidt and the author; also working with them throughout this period as a surgical nurse has been Sister M. Agneta and during the last seven years the author's son, Dr. Ernest V. Smith Jr. This book is the story of the author's boyhood and of his work later in the profession of medicine. His opinions on medical education and medical practice are sound.

Outline of Histology: Part I. General Histology. Part II. Dental Histology and Embryology. By Margaret M. Hoskins, Ph.D., and Gerrit Bevelander, Ph.D., Departments of Anatomy, College of Dentistry and the Graduate School of Arts and Science, New York University, New York. Paper. Price, $2.50. Pp. 179, with 80 illustrations; 112, with 56 illustrations. St. Louis: C. V. Mosby Company, 1942.

This outline of histology is apparently meant as a student aid. Such student aids have, in our opinion, no pedagogical value unless made by the students themselves. A prepared outline does not offer the student an opportunity to train himself in scientific thinking and cannot replace a textbook. But some teachers do not agree with this idea and approve of readymade outlines. They demand, however, that they be short and clear. Both of these qualities are lacking in this book. The text is often inaccurate, and the efforts to explain too much in too brief a span are confusing. The diagrammatic illustrations will not help to give the student much histologic insight. The extensive section on dental histology is somewhat better than the rest of the book. This, however, does not justify the superficial treatment of the outline. It is inferior to other textbooks of dental histology which are available. There is no index.

Fundamentals of Psychiatry. By Edward A. Strecker, M.D., Sc.D., F.A.C.P., Professor of Psychiatry and Chairman of the Department, Undergraduate School of Medicine, University of Pennsylvania, Philadelphia. Cloth. Price, $3. Pp. 201, with 15 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1942.

This little manual is a useful and accurate summary of psychiatry as it is seen through the eyes of a leading specialist. The chapter headings are the usual ones, on etiology, classification of mental diseases, methods of examination and the various types of psychoses. Part of a chapter is devoted to the psychoneuroses, and there is a short chapter devoted to defectives. About seven pages are devoted to some of the neuropsychiatric problems of war. The book is systematic and has a number of good illustrative case histories. It is remarkably complete for its small size.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

AIR EMBOLISM

To the Editor:—**A discussion arose as to what consequences might commonly be expected to follow accidental injection of air into the venous circulation, incident to intravenous therapy. Are there any records as to the approximate amount that has been introduced without developing important reaction?**

Captain, M. C., A. U. S.

ANSWER.—The danger of air embolism during an intravenous drip must be minimal, since 5 to 10 cc. of air has been injected rapidly in man without producing clinical symptoms. The entrance of sufficient amounts of air to produce clinical symptoms requires a gaping of the injured vein and a definite sucking action toward the heart. These factors are present at the large veins of the neck and at the root of the arm (internal and external jugular, subclavian and axillary veins). These veins are fixed by fascial coverings and cannot readily collapse. The placental veins following childbirth and the pulmonary veins, when surrounded by scar tissue, which prevents collapse, are particularly predisposed to permit the entrance and transport of air.

In the case of venous air embolism, a characteristic hissing sound is heard followed by a peculiar churning of the heart. This sound may hardly be heard with the stethoscope but occasionally can be heard at a considerable distance from the patient. When air enters the right side of the heart it is pressed, in the shape of foam or large bubbles, into the pulmonary artery. Death may occur through asphyxia just as in thromboembolism, or dyspnea, cyanosis and tightness of the chest develops, all of which may disappear if the air bubbles are not too obstructive. If the entrance of air is through the pulmonary veins following pleural punctures, pneumothorax or operations on the lung, the air embolus obstructs segments of the arterial tree. The tongue may show pallor; air bubbles can be seen in the retina. Petechial hemorrhages in the skin occur. Blindness, dizziness and convulsions may be present. The administration of 100 per cent of oxygen with a Boothby mask may save life or minimize permanent damage by absorbing the nitrogen bubbles from the vascular tree.

HISTIDINE AND MUCOUS SECRETION IN PEPTIC ULCER

To the Editor:—**On page 345 of your book Selected Questions and Answers it is stated that "Lenormand (*Presse med.* 41:1141 (July 19) 1933) expressed his belief that the beneficial effect of histidine therapy in ulcer was due to its action on the vagus-autonomic system, causing an increased secretion of mucus." Is there available any therapeutic agent with an antihistidine effect, preferably one that specifically neutralizes a supposed (?) excess production of histidine, thus causing a decreased secretion of mucus?**

H. D. Coles, M.D., Chicago.

ANSWER.—There is no evidence to support the view of Lenormand that histidine exerts an effect on the vagus-anatomic system, thereby causing an increased secretion of gastric mucus. Mucus is secreted by the epithelium of the entire surface of the stomach, by the mucoid neck cells of the fundus and by the cardiac and pyloric gland cells. Little is known about the regulation of its secretion, although it is known that mucus is secreted by the resting stomach and that the production of mucus is relatively greatly decreased during the active secretion of hydrochloric acid. In animal experiments, stimulation of the vagus and sympathetic nerves has been shown to result in an increased output of mucus. The injection of epinephrine is followed by secretion of mucus; this secretion is not abolished, however, by the administration of atropine (Portis, S. A.: Diseases of Digestive System, Philadelphia, Lea & Febiger, 1941, p. 100).

There have not been any reports to suggest the existence of any therapeutic agent which diminishes the secretion of gastric mucus. Nor does there appear to exist a substance which may presumably neutralize histidine. Indeed, it has been demonstrated fairly conclusively that histidine does not exert any effect on the volume and acidity of gastric secretion (Chang, Hsiao-Ch'ien: *Proc. Soc. Exper. Biol. & Med.* **37**:155 [Oct.] 1937. Goodman, L. S., and Bearg, P. A.: The Action of Histidine on the Gastrointestinal Tract, *Am. J. Digest. Dis.* **5**:117 [April] 1938. Atkinson, A. J., and Ivy, A. C.: Further Attempts at Achlorhydria, *ibid.* **5**:30 [March] 1938).

It may be stated also that the supposed beneficial effect of histidine in the treatment of gastroduodenal ulcer has not been observed in numerous well controlled experimental and clinical studies. Stalker, Bollman and Mann (*Am. J. Digest. Dis. & Nutrition* **3**:822 [Jan.] 1937) and Sandweiss, Saltzstein and Glazer (*ibid.* **4**:20 [March] 1937), among others, were unable to prevent the development of ulcers in "Mann-Williamson" dogs by the intramuscular injection of histidine. Sandweiss (THE JOURNAL, April 25, 1936, p. 1452) in a careful clinical study of the problem concluded that the transient symptomatic effects of histidine could be explained entirely on the basis of a psychotherapeutic response to hypodermic medication given enthusiastically. Finally, no condition is known in which the secretion of mucus is excessive or in which its inhibition would be desirable.

PROBABLE OVARIAN NEOPLASM

To the Editor:—**A housewife aged 55 complains of intermittent and increasing menorrhagia of one year's duration. Previous to that time she went two to three months without menses on several occasions since the age of 51. She has noticed an increasing size and hardness of the lower part of the abdomen for the past year. Her temperature, pulse and respiration were normal, the blood pressure 230 systolic and 110 diastolic, the weight 149 pounds (68 Kg.). She lost about 40 pounds (18 Kg.) in the past one and one-half years partly through diet. Pelvic examination reveals a protrusion of the cervix about 1½ inches beyond the vaginal introitus without straining. There is some cornification of the mucous membrane but no ulceration or erosion. The cervical canal is about ½ inch in diameter, and a pale, reddish mass about ¼ inch in diameter can be seen attached within the canal to the anterior lip. The uterine "isthmus" is about 1 inch in diameter and about 2½ inches long. In the right side of the pelvis is a mass about 5 inches in diameter, extending into the abdomen to about 1 inch inferior to the umbilicus. The mass is firm, smooth, freely movable and not tender and lies immediately deep to the abdominal wall. It is either a part of the uterine body or is attached to it. In the left side there is another mass which entirely fills this side of the pelvis and extends into the abdomen about 2 inches superior to the left pubic ramus. This mass can be moved but gives the impression of being wedged in the left side of the pelvis. It is firm and rather tender. On its inferior aspect it presents two nodules each about 1 inch in diameter. My diagnoses are hypertension—possibly essential; multiple fibromyomas of the uterus (larger than a four month pregnancy); descensus uteri; cystocele, rectocele and slight urethrocele. However, there are no symptoms suggesting the latter. I should appreciate recommendations as to the handling of this case.**

M.D., Washington.

ANSWER.—One of the first things to think of in a woman 55 years old who bleeds profusely is a granulosa cell tumor of the ovary. The patient may have this condition even if she has uterine fibroids or other neoplasms. Regardless of whether or not a granulosa cell tumor is present, tumors of the size mentioned, especially in a woman of 55, require prompt treatment. In spite of the patient's hypertension it is not advisable to apply radiation therapy, chiefly because it is highly important to make a correct diagnosis. This can be done only by a laparotomy.

The patient should be put to bed for at least a week, preferably longer, with a view to reducing the blood pressure and building up her resistance as much as possible. All the necessary laboratory tests should be made and she should be given repeated small doses of a sedative such as phenobarbital to help reduce the blood pressure. She may also be given large amounts of vitamin C in addition to a well rounded diet. If the red blood cell count is below normal it should be increased, by transfusion if necessary. Consultation should be had with a physician anesthetist concerning preoperative medication and also the safest anesthetic to use. If possible an internist should be present at the operation, and certainly all paraphernalia and medication should be at hand for the treatment of shock or any other complication. The physician assistants and nurse should be familiar with the surgeon's technic so that there will be a minimum of motions, confusion and delay. It is essential to remove the neoplasm as speedily as possible and with the least amount of trauma. No effort should be made to repair the relaxed vagina. At the time of suturing the cervical stump (if a supravaginal hysterectomy is performed) or closing the vaginal vault (if a total hysterectomy is done) the bladder can be advanced so as to take up part of the vaginal relaxation. A much better procedure is to sew the cervical stump or the vaginal vault to the fascia of the rectus muscles. Anchoring the vaginal vault to the abdominal vault should correct the prolapse. In nearly all cases in which such a suspension is performed, a perineorrhaphy must also be carried out, but in this

case only the abdominal operation should be done and not the vaginal. The shorter the operation and the period of anesthesia, the safer it will be for the patient.

In a case like this it is best to remove the entire uterus and both tubes and ovaries not only because of the strong likelihood of a malignant growth in the ovaries or uterus but also because there is a large polyp or pedunculated, submucous fibroid in the cervical canal.

If the surgeon is not capable of performing a total hysterectomy with ease and rapidity, he should ask some one else, preferably an experienced gynecologist, to do the operation. The patient's life will depend in large measure on the skill of the operation, and she should have the best possible care.

If the vaginal prolapse is present after the abdominal operation, a pessary may be inserted in the vagina or a plastic operation may easily be done under direct infiltration anesthesia a few months after the laparotomy, provided of course the patient's general condition will permit the operation.

PERSISTENT ULNAR NERVE PAIN AFTER CONTUSION

To the Editor:—A patient injured his elbow as a result of a fall. He is a carpenter, and the handle of the hammer is supposed to have struck the elbow in the course of the fall. About two months ago the ulnar nerve was moved from its original position behind the internal condyle and deposited in a new bed in front of the condyle. This operation was done because of a diagnosis of chromatic neuritis. The patient has continued to have more pain than he had previous to it, even after a period of two months. At operation the sheath of the nerve was also dissected free for a space of approximately 1½ inches. The surgeon evidently thought that the trauma had injured the nerve sheath and that there was some constriction that accounted for the pain. The problem which I have to decide is whether or not I have to operate again and transfer the nerve to its original bed. I think it is possible that the new position of the nerve causes it to be stretched unduly and may have something to do with the continuation of the pain. Diathermy and other forms of heat application have not given good results, nor has massage.

P. H. Owens, M.D., Kansas City, Mo.

ANSWER.—On the basis of the information submitted, the only explanation which can be suggested for the pain in the ulnar distribution is that the nerve was contused and the neuralgia is at the point of contusion, although the nerve was probably not divided. There would be nothing gained or lost by restoring the nerve to its original position. If a neuroma cannot be found on exposing the nerve it would probably be better to divide the nerve, on condition that the pain is bad enough to warrant this procedure. If a neuroma can be found, it should be resected and the nerve resutured.

IDENTIFICATION OF RETAINED PLACENTAL TISSUE

To the Editor:—Given a case of spontaneous, subacute inversion of the uterus, a curettage was done to determine the possible retention of placental tissue. Is an obstetrician justified in stating that he can recognize with certainty, with the naked eye, placental tissue in the form of uterine curettings, or must it always be confirmed by microscopic findings of chorionic villi?

M.D., New York.

ANSWER.—Placental tissue can usually be determined with the naked eye, particularly in the early weeks of pregnancy. A simple way to verify the presence of placental villi is to immerse a portion of the tissue in water. If villi are present they will stand out prominently. At or near term a firm blood clot removed by curet may be mistaken for placental tissue, but by breaking up the clot one may easily determine the true condition. Occasionally a piece of thick decidua is mistaken for a piece of placenta containing villi. In such a case, if the water immersion test does not help, a hand lens almost certainly will. When a curettement is not performed until days or weeks after a miscarriage or full term labor, a hard hemorrhagic piece of tissue is often removed, the contents of which can be determined only by microscopic examination.

INTRANASAL INSULIN ADMINISTRATION

To the Editor:—In August 1936, there was an article in The Journal regarding the experiments of Ralph H. Major, M.D., in the use of intranasal applications of insulin. Please advise me if this experiment was carried further and with what results.

R. W. Holley, M.D., Appalachia, Va.

ANSWER.—Some 25 patients with diabetes of moderate severity have been treated by intranasal application of insulin and there is no doubt that they can be controlled by this method. It has been abandoned for two reasons: First, it proved to be an expensive method of administration because the doses were necessarily larger than those effective with hypodermic medication. Second, most of the patients after a time grow tired of the frequent nasal spray and prefer to return to subcutaneous administration.

ULTRAVIOLET LAMPS IN SCHOOLS FOR PREVENTION OF INFECTIONS

To the Editor:—I should like to ask about the advisability of installing special ultraviolet ray lamps in our centralized school for the prevention of air borne infections. The literature on this subject seems promising, but questions have arisen as to whether there would be any harmful effects from the ultraviolet rays, such as injury to the eyes or skin cancer.

M.D., New York.

ANSWER.—There is not sufficient evidence to sponsor unreservedly the use of ultraviolet lamps in schools for the prevention of air borne infections. Nevertheless it is well known that ultraviolet emanations of selected ray lengths are bactericidal at short distances. In the application of this knowledge to school buildings, the installations should be such as to rule out any likelihood of injury to the eyes, skin burns or like hazards.

DISPOSITION OF RADIUM SUPPLY WHILE IN MILITARY SERVICE

To the Editor:—If I enter military service, I must put away for the duration about 100 mg. of radium. I do not wish to keep it around my small home, for I have learned that, lead or no lead, it darkens film within a few days, and I don't wish it near my children. What do you suggest as a means of disposing of it safely for an unpredictable length of time until I return to practice?

M.D., Missouri.

ANSWER.—The best disposal of radium during the war is to keep it in use in treatment of the sick. There should be an attempt to make arrangements with a responsible man to store and use the radium in his own practice, at the same time getting authority to do so from your insurance company. Caution must be used in choosing a physician who already uses radium and is skilled in its use and care. Someone may be found who needs an extra supply and who would be willing to pay something for its use, at least the insurance premium.

BIOPSY OF PROSTATE THROUGH RECTAL WALL

To the Editor:—At a recent meeting of our tumor board we discussed a case in which a suggestive nodule in the prostrate was easily accessible to palpation on rectal examination. One physician of some years of experience advised taking a biopsy through the rectal wall, stating that the idea that one should not go through the rectal wall was nonsense and an idea which physicians have handed down without foundation. If this is true, some of us who expose the prostate through a perineal incision to take such biopsies are making rather hard work out of what could be an easy and minor procedure. I would appreciate an opinion on this subject.

J. Robert Rinker, M.D., Fort Worth, Texas.

ANSWER.—A biopsy made through the rectum into the prostate is not good surgery. Such penetration of the bowel can result in infections.

STABILITY OF SOLUTION OF SODIUM SULFATHIAZOLE

To the Editor:—Please advise how long solution of sulfathiazole is stable and potent.

J. J. Johnson Jr., M.D., Las Vegas, N. M.

ANSWER.—The solution of sulfathiazole must mean a solution of the sodium salt. Although it is not known how long such a solution will be stable, it is advisable to use only freshly prepared solutions for injection. In alkaline solution the sulfonamides are readily oxidized and may yield toxic products.

ENDOCRINES AND CARCINOMA

To the Editor:—Has orchiectomy or diethylstilbestrol proved to be of any value in the treatment of neoplasms other than carcinoma of the prostate?

L. A. Crowell Jr., M.D., Lincolnton, N. C.

ANSWER.—The employment of either orchiectomy or diethylstilbestrol in the treatment of carcinoma of the prostate is still on an experimental basis. There is no reason to believe that these procedures are of any use for other types of neoplasms.

VITAMIN A AND COLOR BLINDNESS

To the Editor:—In Queries and Minor Notes in The Journal, Nov. 28, 1942, page 1080, the answer to M.D., New Mexico, relative to color blindness, does not mention the two reports of Dunlap and Loken concerning the possible value of vitamin A in treating color blindness (Science 95:554 [May 29], 96:251 [Sept. 11] 1942). Granted that this is not a completely studied problem, perhaps the inquirer would like to know of the references. It seems too bad that the soldier spoken of should lose his chances for advancement if there is any type of treatment available that might possibly be of benefit, even though experimental in character. The doses of vitamin A recommended by Dunlap and Loken do not appear to be sufficiently high to fall within a toxic range.

C. G. Weigand, M.D., Indianapolis.